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ELECTROENCEPHALOGRAPHIC EVIDENCE OF PERSONALITY CHANGES PRODUCED BY ATARAXIC DRUGS IN MENTALLY DISTURBED PATIENTS.

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DURING routine electroencephalographic examinations of psychotic patients, many tracings were marred by electrical artefacts resulting from muscular movements, with the consequence that the recordings became unsuitable for diagnostic purposes. In those cases we used to prescribe chlorpromazine or reserpine as sedatives, and the patients were asked to return for another electroencephalographic recording when they were in a more accommodating frame of mind. Thus a small collection of electroencephalographic tracings, before and after the administration of one of the two drugs, was obtained by chance.

On another occasion we took electroencephalographic recordings of six chronic schizophrenic patients before and after the administration of five milligrammes of reserpine, looking for the appearance of suspected sleep patterns. These did not appear, but the electroencephalographic recordings were filed for future reference.

In addition, we had investigated the effect of benactyzine, which, according to Danish workers, was alleged to abolish α-activity. This, we thought, might give us a clue about the psychological significance of the α waves. Three patients and the writer took various amounts of benactyzine ("Suavitil"), and characteristic psychological changes were noted, together with a variation of the α-rhythm in the electroencephalographic tracings. We made the surprising discovery that therapeutic doses of benactyzine seemed actually to increase the α-activity in areas where it had previously been poor. Only large, almost toxic, doses decreased the α-rhythm.

This observation induced us to reexamine our old electroencephalographic recordings of patients who had received reserpine or chlorpromazine, and we noted that the α-rhythm was activated in areas where it had previously been scarce. This applied particularly to the temporal regions.

We next selected two patients, one with habitually stable α-activity and another with no α-activity at all, and gave them five milligrammes of reserpine and took their electroencephalographic tracings.

Meanwhile, we happened to take the electroencephalographic tracings of a hyperactive epileptic child before and after a change of environment which had resulted in a temporary relief in the behaviour difficulties. We found that the improvement of behaviour, due to the environmental factor, produced α appearance in the temporal

regions similar to that experienced with the ataraxic drugs.

In the 14 cases we had investigated, clinical follow-up examination showed that the changes observed in the electroencephalographic tracings were of prognostic value. It appeared that the appearance of a stable α-rhythm in the temporal regions where, before the administration of ataraxics, it had not been present, was of good prognostic import. This led us to investigate the finding further.

Methodology.

We attempted to investigate whether the ataraxic drugs produced stable α-activity, particularly in the temporal regions, and how far such a phenomenon correlated with psychological, physiological and clinical changes.

We classified the α-rhythm, according to the intensity of its activity, from "absence of α" through "scarce α", "intermittent bursts of α", "low-voltage continuous α" (less than 25 millivolts) and finally to "high-voltage continuous α" (more than 50 millivolts).

The clinical effect of the ataraxic drugs on patients, over a follow-up period of not less than two months, was also classified on a scale from "no improvement", through "slight improvement", to "moderate improvement" and, finally, to "considerable improvement".

Findings.

Our results are demonstrated in Tables I and II.

Table I summarizes the electroencephalographic and clinical changes of our 14 patients before and after the administration of ataraxic drugs.

Table II summarizes the effect of benactyzine on the electroencephalograms of three patients, together with a personal investigation by myself.

Analysis of Data.

Relationship between Change in α-Activity and Clinical Effect.

The effect of chlorpromazine, reserpine, "Pacatal" and "Nutinal" on the α-rhythm and their clinical effects in terms of sociability of the patients is as follows:

1. A survey of the results (Table I) demonstrates that, with the administration of ataraxics, patients can be defined into two categories: those who respond with an increase in the amount and stability of α-rhythm, and those who do not (Figures I, II and III).

2. Out of eight patients showing the increase in α-activity, four were considerably and four were moderately improved.

3. Out of five patients showing no increase of α-activity, two were clinically not improved at all and three were slightly improved, whilst none could be regarded as moderately or considerably improved.

Significance of Appearance of Temporal α-Rhythm.

Table I shows that many psychiatric patients may have some α-activity in the parieto-occipital regions and none

TABLE I.

Effect of Ataraxics on Stability of Alpha Rhythm.

Case No.	Age. (Yrs.)	Sex.	Psychiatric Condition.	Treatment.	Regional Effect on Alpha Activity.			Follow-up Clinical Effect in Terms of Sociability.
					Temporal.	Parieto-occipital.	Frontal.	
I	14	F.	Psychopathic, violent episodes.	Reserpine, 5·0 milligrammes.	Change from absent or scarce to stable α-rhythm.	Change from intermittent to continuous.	No change; some α-rhythm.	Moderate improvement.
II	47	M.	Chronic schizophrenia.	Reserpine, 5·0 milligrammes.	Change from absent to stable α-rhythm.	Change from low to high voltage.	Change from absent to stable α-rhythm.	Considerable improvement; on trial leave.
III	56	M.	Chronic schizophrenia.	Reserpine, 5·0 milligrammes.	Change from low to high voltage.	(Electroencephalogram not available.)	(Electroencephalogram not available.)	Considerable improvement.
IV	28	M.	Chronic schizophrenia.	Reserpine, 5·0 milligrammes.	Change from medium to high voltage.	(Electroencephalogram not available.)	(Electroencephalogram not available.)	Moderate improvement.
V	28	M.	Chronic schizophrenia.	Reserpine, 5·0 milligrammes.	(Electroencephalogram not available.)	No change; low voltage α-rhythm.	No change; no α-rhythm.	No improvement.
VI	37	M.	Chronic schizophrenia.	Reserpine, 5·0 milligrammes.	(Electroencephalogram not available.)	No change; stable α-rhythm.	No change; occasional α-rhythm.	Slight improvement with chlorpromazine.
VII	21	M.	Chronic schizophrenia.	Reserpine, 5·0 milligrammes.	No change; stable α-rhythm.	No change; stable α-rhythm.	Change from absent to occasional α-rhythm.	Slight improvement.
VIII	32	M.	Chronic schizophrenia.	Reserpine, 5·0 milligrammes.	(Electroencephalogram not available.)	Slight change from "choppy" to smooth α-rhythm.	No change; occasional α-rhythm.	No improvement.
IX	45	F.	Involutionary depression *plus* organic frontal deterioration.	"Pacatal", 150 milligrammes.	Change from absent to low voltage stable α-rhythm.	No change; absent α-rhythm.	No change; absent α-rhythm.	Moderate improvement.
X	11	M.	Behaviour disorder, *plus* epilepsy.	Chlorpromazine, 100 milligrammes.	Change from absent or scarce to stable α-rhythm; epileptic spikes unchanged.	No change; stable α-rhythm; epileptic spikes unchanged.	No change; occasional α-rhythm.	Considerable improvement.
XI	18	M.	Schizophrenia.	Benactyzine, 4·0 milligrammes.	Change from sharp, poorly organized to round, better organised α-rhythm.	No change; sharp, poorly organized α-rhythm.	No change; occasional α-rhythm.	Slight improvement with chlorpromazine.
XII	41	F.	Neurasthenia.	Benactyzine, 8·0 milligrammes.	Change from low to high voltage stable α-rhythm.	Change from sharp to smooth α-rhythm.	No change; occasional α-rhythm.	Moderate improvement with "Nutinal".
XIII	41	F.	Psychoneurosis.	Benactyzine, 4·0 milligrammes.	Change from absent to high voltage stable α-rhythm.	Change from stable "choppy" to high voltage smooth α-rhythm.	(Electroencephalogram not available.)	Considerable improvement with chlorpromazine.
XIV	8	F.	Hyperkinetic epilepsy.	Change of environment.	Change from low to high voltage stable α-rhythm.	No change; stable α-rhythm.	No change; stable α-rhythm.	Considerable temporary improvement.

in the temporal regions. In those cases the α-activating effect of the ataraxic drugs is dramatically pronounced in the temporal regions specifically, which suggests that it is of clinical psychiatric significance (Figure IV).

Benactyzine.

Attention should be drawn to the fact that benactyzine, in therapeutic doses, produced the characteristic stabilization of the α-rhythm as seen with the other ataraxic drugs. In larger doses, which must be considered to be approaching toxic level, the α-rhythm undergoes the change reported by overseas observers O. O. Jensen and I. Ostenfeld (1955), in that the α-rhythm is abolished. This is generally not realized (Figures V and VI).

Discussion.

The foregoing data suggest that chlorpromazine, reserpine, "Pacatal" and small amounts of benactyzine produce "good" α-activity in patients who have habitually little or none, improve α-activity in patients with "poor" α-rhythm, and have no effect on patients with habitually "good" α-activity. The production of good α-rhythm, if present, is most pronounced in the temporal regions. When α-activity is intermittent, occasional, or absent, and when, in these cases, ataraxic drugs produce good α-activity, the best clinical results are produced; when there is a "good" α-activity to start with, little or no improvement can be expected with ataraxics. Thus there seems to be an important correlation between change towards a stable α-rhythm and clinical improvement.

Some psychiatric patients have no α-activity in the temporal regions, though there may be considerable α-activity in the parieto-occipital regions, and it is the appearance of α-activity in the temporal regions which correlates with clinical improvement, whether as a result of the administration of ataraxic drugs or otherwise (Figure VII).

On the other hand, the ingestion of large amounts of benactyzine, resulting in diminished voltage or abolition of the α-activity, seems to produce extreme emotional blunting, as well as intellectual impairment and retardation.

All these observations and inferences are only suggestive; they are by no means conclusive. The experimental procedures must suffer from the criticism that many relevant factors were uncontrolled. For instance, the varying temporary mental states of the patients during the electroencephalographic recordings were not considered at all, though it is known that apprehension, anxiety, mental effort, imagery and intellectual activity are able to "block" α-activity. The serial effect of the first on a subsequent electroencephalographic recording has not been taken into account. The patient is usually more apprehensive during the first recording, when he often suspects that he is going to be given electroconvulsive therapy or be electrocuted, than during the second recording, when he feels assured that nothing is going to happen to him and that he can relax. This relaxtion is known to be conducive to α-activity. The clinical improvement noticed in the patients may not always have been due to the effect of the ataraxic drugs, but may have been the result of social and occupational therapy which were applied at the same time. This was particularly evident in Case XI; the patient was slightly improved with chlorpromazine therapy alone, but improved still further when he underwent an additional course of rehabilitation. There were other, though less relevant, uncontrolled factors which, theoretically, could have vitiated our findings. Still, it must be recognized that many serial electroencephalographic examinations of other psychiatric patients were coincidently being conducted in our electroencephalographic department, and none of them showed relevant serial changes in the patients' α-patterns. The additional effect of social and occupational therapy may diminish the force of the inference that in all cases in which considerable improvement occurred, it was caused by the ataraxic drugs only; but this would reinforce the argument that those who did not show any changes in their α-activity were poor subjects for ataraxic therapy alone. On the basis of previous practical clinical experience we are inclined to consider the findings, in relation to the general effect of ataraxic drugs, as probably significant.

There already exists a considerable literature on the effects of chlorpromazine, reserpine and benactyzine on the electroencephalographic pattern. Most workers, using animals or human epileptics as experimental subjects, ignored their habitual α-pattern. The following workers, for instance, have published findings about the effect of

TABLE II.

Effect of Increasing Doses of Benactyzine on the Electroencephalogram.

Dosage. (Milligrammes.)	Case Number.	Age. (Years.)	Sex.	Psychiatric Condition.	Regional Effect on Alpha Activity.			Clinical Effect.
					Temporal.	Parieto-occipital.	Frontal.	
4·0	XI	18	M.	Schizophrenia.	Change from sharp, poorly organized to round, better organized α-rhythm.	No change. Sharp, poorly organized α-rhythm.	No change. Occasional α-rhythm.	Not tested.
	XIII	41	F.	Psychoneurosis.	Change from absent to high voltage stable α-rhythm.	Change from "choppy" to high voltage, stable α-rhythm.	(Electroencephalogram not available.)	Not tested.
8·0 to 9·0	XI	18	M.	Schizophrenia.	Change from sharp, poorly organized to better organized, lower voltage α-rhythm.	Change from sharp, poorly organized, to sharp, stable α-rhythm.	No change; occasional α-rhythm.	Not tested.
	XII	41	F.	Hypochondria.	Change from low to high voltage, stable α-rhythm.	Change from sharp, high voltage, to smooth, low voltage, stable α-rhythm.	No change; occasional α-rhythm.	Not tested.
	Present writer	43	M.	—	Change from high voltage, stable, to low voltage, unstable α-rhythm.	Change from stable to intermittent α-rhythm.	Change from occasional to stable α-rhythm.	(i) Severe emotional blunting. (ii) Loss of feeling and drive. (iii) Mild intellectual deterioration.
12·0	XI	18	M.	Schizophrenia.	Return to poorly organized α-rhythm.	Return to poorly organized α-rhythm.	No change; some α-rhythm.	Not tested.
20·0	XI	18	M.	Schizophrenia.	Suppression of almost all α-activity. Slow and fast waves.	Suppression of almost all α-rhythm. Slow and fast waves.	Suppression of occasional α-rhythm.	(i) Total apathy. (ii) Retardation. (iii) Marked intellectual deterioration.

chlorpromazine on the electroencephalographic pattern: Hiebel, Bonvallet and Dell (1954); Terzian (1954); Hippius, Mellin and Rosenkoetter (1954); Chagass (1955); Pupo, Zukerman and Longo (1955). The following workers have published findings about the effect of reserpine on the electroencephalogram: Chen and Ensor (1955); Dennison, White, Moore and Pierce (1955). All of them found only minor electroencephalographic changes, and often came to different conclusions on details. Reports about the effect of benactyzine on the electroencephalographic pattern were made by the Danish workers Jensen (1955) and Ostenfeld (1955). However, they considered only the α-diminishing effect and ignored the α-activating effect of small doses.

Few workers have observed the electroencephalographic effect of these drugs on psychiatric patients. Liberson (1955), studying the effect of chlorpromazine on the electroencephalographic tracings of schizophrenic patients, observed that there was a tendency towards increased α-continuity, a slightly decreased α-frequency and the appearance of α-activity in the frontal regions. Goldman and Balzhiser (1955) found a tendency towards an increase in the amount and voltage of the α-rhythm, the appearance of bilateral differences, and a decrease in the δ-activity. Turner and Berard (1954) have published observations relevant to our work. They term tracings in which α-rhythm is broken up by cortical activity, "desynchronized". They have found that in such desynchronized patients chlorpromazine causes the appearance of rhythmical α-activity and diminution of response to nociceptive and emotional stimuli. They related these observations to their clinical findings.

Psychological Implications.

If we want to understand the significance of the electroencephalographic changes brought about by chlorpromazine or reserpine, we shall have first to understand the meaning of habitually poor or stable α-activity in a person. What is the difference between some people having habitually poor α-activity and others having habitually good α-activity?

A great number of psychologists have tried to answer this question.

Saul and Davis (1939 and 1949) established that an habitually regular and persistent α-rhythm was found exclusively in subjects with a passive and dependent personality. Subjects with absent, scarce or intermittent α-rhythm were usually domineering, competitive personalities. The work of Saul and Davis was repeated and checked by Harris (1952) and by several other workers. Ellingson (1956), when summarizing the evidence supporting the theory of Saul and Davis, stated that it is now generally accepted. The relevance of the work of Saul and Davis to our observations is obvious. These workers compared a cross-section of a population of passive personalities with high α-activity with another population of competitive personalities with little α-activity. We observed how chlorpromazine and reserpine changed the personality of the same subject, together with his habitual electroencephalographic pattern, and how the tense, competitive personality became passive and dependent, the change being correlated with a change of low into high α-activity in his electroencephalogram.

Grey Walter (1943) found that subjects having low α-activity, though their minds were at rest, were intense

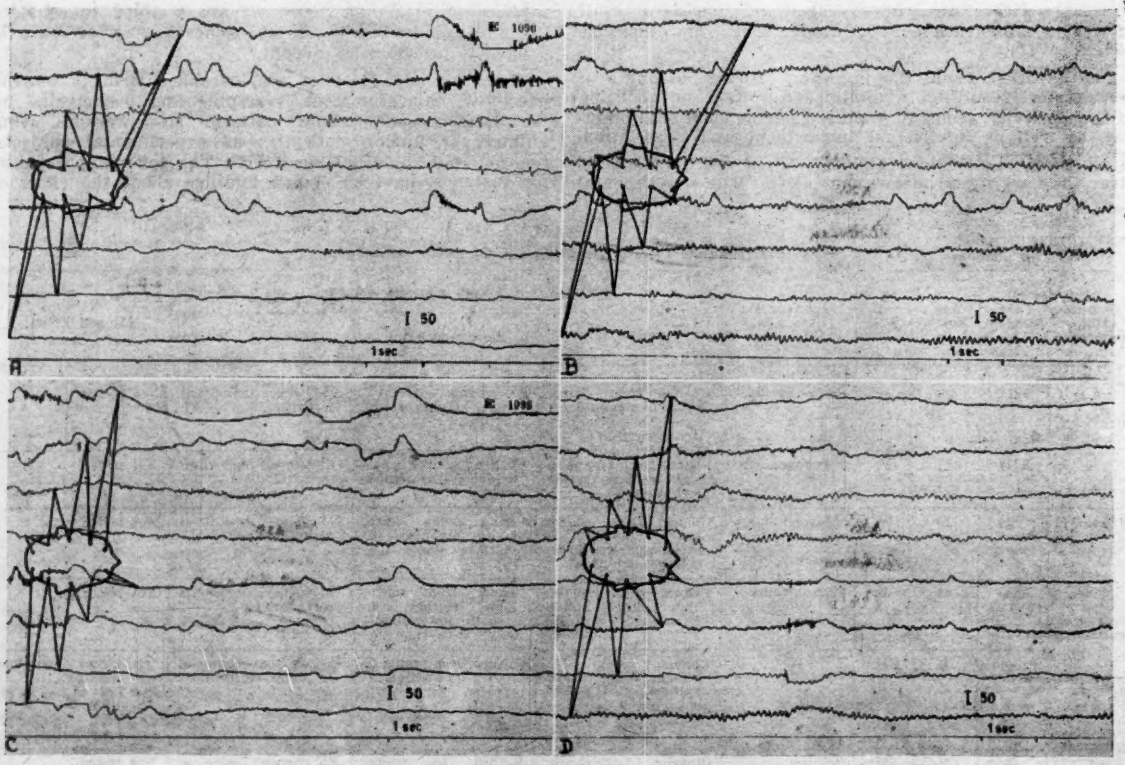

FIGURE I.

Case II. This demonstrates the change towards a stable α-rhythm in both median (A and B) and temporal (C and D) regions. The spikes in the tracings in A are arterial artefacts. A: Before "Serpasil" (median localization). B: After "Serpasil" (median localization). C: Before "Serpasil" (temporal localization). D: After "Serpasil" (temporal localization).

visualizers. Other subjects, having high α-activity even when their minds were at rest, were non-visualizers. We did not test whether our patients, under the effect of the drugs, had changed from visualizers to non-visualizers.

with little or no α-activity about their habitual mental habits. They all stated that they were thinking or imagining something all the time; there was always something on their minds. They felt more relaxed and were

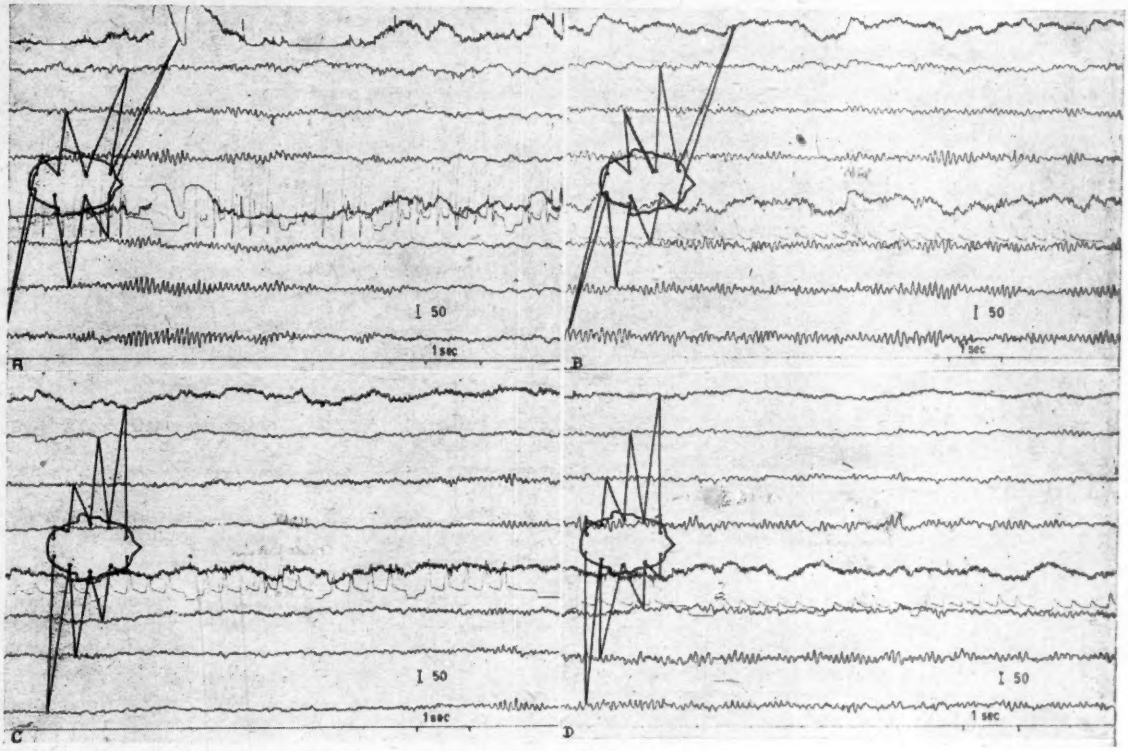

FIGURE II.

Case I. This demonstrates the general change towards a stable α-rhythm. A: Before "Serpasil" (median localization). B: After "Serpasil" (median localization). C: Before "Serpasil" (temporal localization). D: After "Serpasil" (temporal localization).

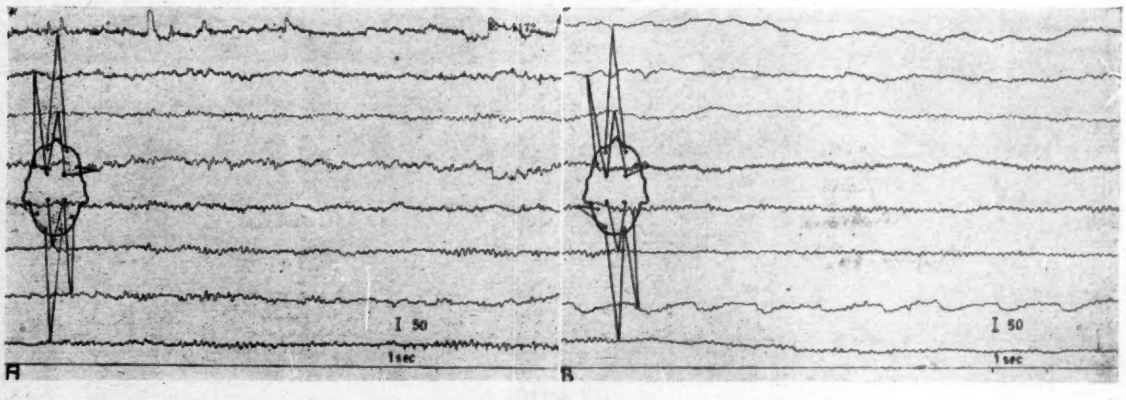

FIGURE III.

Case VIII. This demonstrates that "Serpasil" has no effect on the α-rhythm in patients who habitually have a stable α-rhythm. A: Before "Serpasil". B: After "Serpasil".

Ostow (1950) found that α-activity generally corresponded to a preparation for constructive thinking, and that such α-activity disappeared when the constructive process was put into action. We asked a few patients

habitually less ruminative after the administration of ataraxic drugs.

We thus believe that the ataraxic drugs diminish the autistic imagery of psychotic patients, making them

thereby susceptible to normal outside influences and enabling them to give up their rigid ruminating preoccupied mental patterns.

Physiological Implications.

Little work seems to have been done by physiologists to explain the difference between scanty and continuous

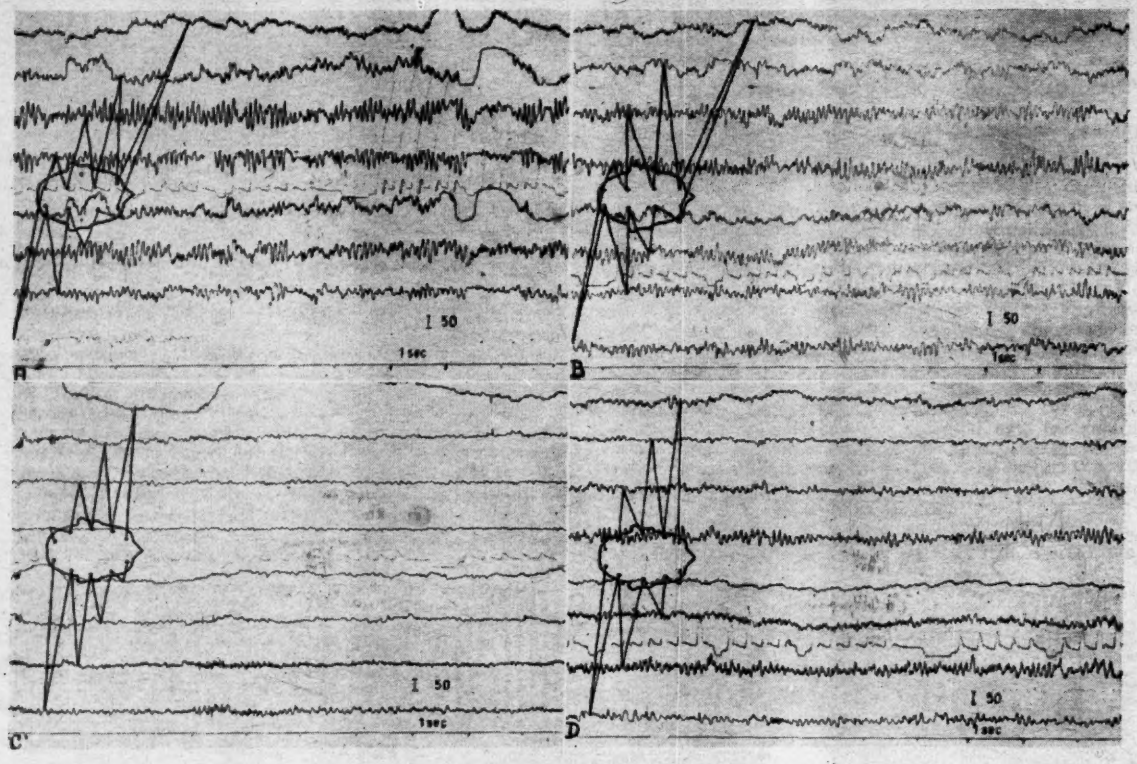

FIGURE IV.

Case X. This demonstrates that the change towards a stable α-rhythm is localized to the temporal region. A: Before "Largactil" (median localization). B: After "Largactil" (median localization). C: Before "Largactil" (temporal localization). D: After "Largactil" (temporal localization).

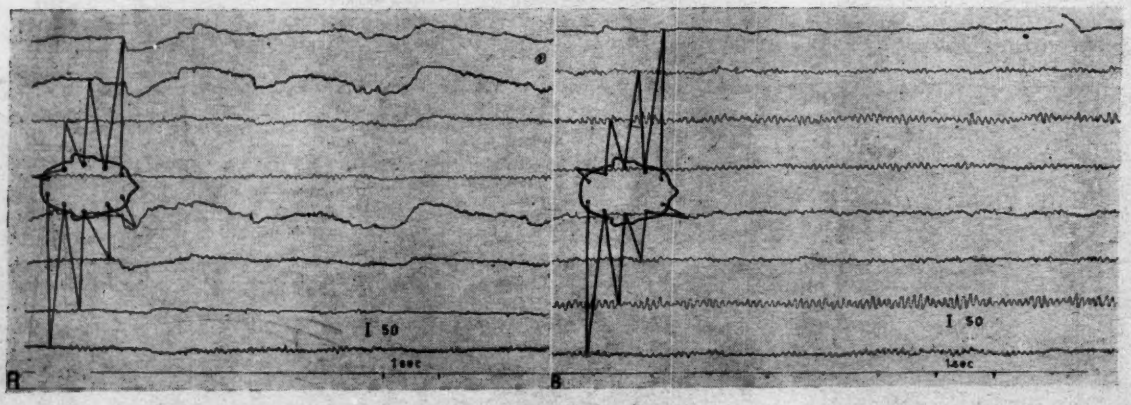

FIGURE V.

Case XII. This demonstrates the general change towards a stable α-rhythm produced by small amounts of "Suavitil". A: Before "Suavitil" (temporal localization). B: After "Suavitil", four milligrammes (temporal localization).

We found no references in the literature to our observation that it is the localization of changes in the temporal region which is so significant in the determination of changes of behaviour patterns.

α-activity in electroencephalographic tracings. Reference has not been made to the fact that electroencephalographic changes, localized to the temporal area, would have important relations with the mesial and basal structures

of the temporal lobe, which are known to contain important emotional centres.

Hill (1950) summarizes the findings of several authors who were working among schizophrenics, and who suggested that the habitually scarce or continuous α-activity could be an indication of the degree of abnormality of the physiological behaviour of the cortex. This may apply to Case V, in which the patient's low-voltage α-activity was not affected by reserpine. On the administration of an ataraxic drug to a patient suffering from Huntington's chorea, whose electroencephalogram showed complete absence of α-activity, no α-activity appeared and the tracings remained completely flat. It is presumed that the absence of α-waves in Huntington's chorea is due to

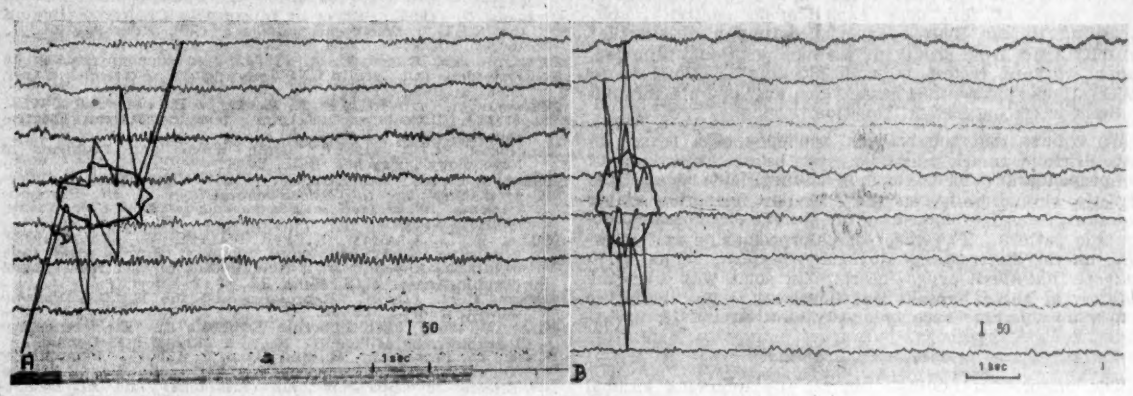

FIGURE VI.

Case XI. This demonstrates that larger amounts of "Suavitil" suppress the α-rhythm. A: Before "Suavitil". B: After "Suavitil", 20 milligrammes.

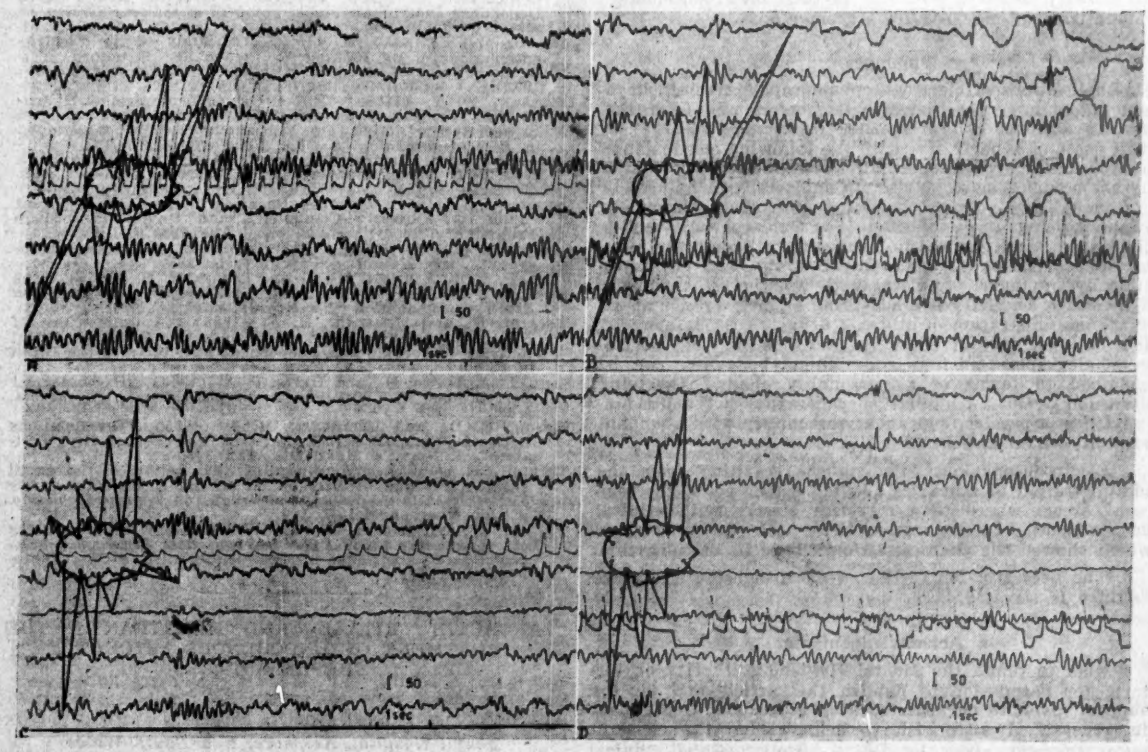

FIGURE VII.

Case XIV. This demonstrates that psychological adjustment also produces changes towards a stable α-rhythm localized in the temporal region. This patient did not receive any drugs. A: Before change of environment (median localization). B: Patient emotionally adjusted after change of environment (median localization). C: Before change of environment (temporal localization). D: Patient emotionally adjusted after change of environment.

organic changes in the brain. We think that, in this case, the hypothesis of the above-mentioned workers may have some justification.

The general effects of benactyzine on the central nervous system have, to our knowledge, not been investigated. Large doses of this drug can abolish α-activity, and, according to our limited experience, impair intellectual capacity apart from producing extreme emotional blunting. Other workers record "thought-blocking". Both these observations suggest that benactyzine may operate through a direct effect on cortical function.

We believe that the habitual tendency of a person to have little or much α-activity may be an expression of the preponderance of one or more natural hormones acting, directly or indirectly, on the reticular formation which is known largely to determine the specific electroencephalographic pattern. The effect of chlorpromazine and reserpine on the electroencephalographic pattern tempts us to suggest that these drugs interfere in some way with the balance of these hypothetical hormones. We intend to follow up this clue experimentally at a later date.

Clinical Applications.

The provisional findings suggest the following clinical possibilities.

1. Patients having little or no α-activity are likely to benefit by the administration of ataraxic drugs, while those having habitually stable high-voltage α-activity are not.

2. Patients undergoing a course of ataraxic drugs and still showing deficient α-activity in their electroencephalographic tracings may require a greater dose.

Summary.

1. Observations of electroencephalographic tracings have been made in 14 psychiatric cases, before and after the administration of chlorpromazine, reserpine, "Pacatal" or small doses of benactyzine, with the following conclusions: (*a*) In subjects with habitually scarce α-activity the α-rhythm becomes more stable. In subjects with habitually continuous high-voltage α-activity the electroencephalographic tracings are unaffected. (*b*) Subjects with habitually scarce α-activity, which changes to full α-activity after the administration of the ataraxic drugs, are benefiting clinically by them. Subjects with habitually continuous high-voltage α-activity are benefiting slightly or not at all by the administration of ataraxic drugs. (*c*) The correlation between the effect of these drugs on the electroencephalographic tracings and clinical behaviour can be explained in terms of a personality change, involving alteration from a ruminative personality with little α-activity to a passive, dependent personality with abundant α-activity (Saul and Davis, 1949).

2. Electroencephalographic changes resulting from the administration of ataraxics should be focused to the temporal areas, where they correlate closely with clinical improvement. In some cases these were the only areas which showed the characteristic changes in the α-rhythm.

3. The necessity for further work to substantiate these findings is stressed.

Acknowledgements.

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"LARGACTIL", "RITALIN" AND "MERATRAN" IN THE TREATMENT OF ENDOGENOUS PSYCHOTIC DEPRESSION.

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DURING the past two and a half years I have used many drugs, either alone or in combination, in an endeavour to determine the most rapid and efficacious method of treating acute mental illness. In this article I shall refer to one particular facet of psychotic illness—the depressive phase of the manic-depressive psychosis—and submit an alternative method of treatment to the almost universally used electrotherapy.

Two objectives have been kept constantly in view: (i) the possibility of achieving with new drugs remissions of a more permanent nature than those obtained with former therapies; (ii) the possible elimination of electrotherapy as the basic method for treating psychotic illness in a mental hospital setting.

Most psychiatrists experience little difficulty in recognizing psychotic depression. The only point which may be difficult to decide is whether the depression is basically a thymergasia, or whether it is depression accompanying schizophrenia—schizo-affective depression. In any case, most psychiatrists use electrotherapy to treat both, and it is only the prognosis that differs.

In the light of electroencephalographic studies of the effects of new drugs, it appeared that there should be a rational therapeutic method of treating psychotic depression in the same manner as manic states, which are rapidly relieved by the exhibition of chlorpromazine. As has already been mentioned in a previous article (Morgan, 1956*b*), I was, at first, disappointed with the action of chlorpromazine in depressive states. It was surprising that although manic states, almost without exception, responded well to chlorpromazine, the results with patients suffering from depression were most unpredictable; some patients improved rapidly, whilst others showed little or no response at all. Recourse would then have to be made to electrotherapy.

With the advent of the psycho-analeptics or anti-depressant drugs pipradrol ("Meratran") and phenidylate ("Ritalin"), it seemed that the answer might be at hand with regard to the treatment of psychotic depression. However, again I was disappointed, for whilst mild depressive states and neurotic and reactive depressions were frequently promptly ameliorated, the hard core of acute endogenous depression remained unaffected.

The next step was to combine these two drugs with chlorpromazine. The results achieved by the combination were much superior to those obtained by using the drugs separately. Initially, the "Meratran" used was supplied through the generosity of the William S. Merrell Company, of Cincinnati, Ohio, and the "Ritalin" by Ciba, Australasia, Proprietary, Limited. Unfortunately I had only sufficient "Meratran" to treat 40 patients (the results in this series have already been published—Hilliard, 1956), so that the bulk of my experience has been gained with "Ritalin". My belief is that "Ritalin" is the more efficacious of the two drugs, but this may well be because I have used "Ritalin" more extensively. It is interesting to note that "Meratran" may perhaps produce undesirable side effects, such as the occurrence of hallucinations (Schou, 1956); but in my experience, and with the levels of dosage that I have used, there have been no side effects.

Dosage and Side Effects.

It has been customary to treat patients suffering from acute psychotic depression with 400 to 800 milligrammes of chlorpromazine per day initially, combined with either 10 to 20 milligrammes per day of "Meratran" or 40 to 60 milligrammes per day of "Ritalin". As the patients start to show improvement, the dosage of chlorpromazine is lowered to 100 to 300 milligrammes per day. When the patients are well enough to proceed on leave from the hospital, and if it seems advisable, they are given a prescription for chlorpromazine and "Ritalin", the dosage of the latter usually being two tablets in the morning and two at 2 p.m. With the patients away from the hospital on out-patient status, there is less tendency for them to relapse and return to hospital, as is frequently the case when patients are treated with electrotherapy alone. My practice has been to discontinue the drugs six to nine months after the majority of patients leave hospital; but in some cases it seems wise to continue treatment for an even longer period.

Side effects have been virtually non-existent. However, although I have seen no case of agranulocytosis among any of the patients I have treated, there is always the possibility that this may occur when any phenothiazine derivative is administered, especially in small sensitizing doses. Vigilance is required to avoid this complication.

However, there is one side effect of both chlorpromazine and reserpine which, I believe, may yet prove to be the most serious long-range complication of therapy. It is the tendency shown by at least one-third of the patients who are given ataractic drugs to gain weight. This weight gain is at times considerable, and proves to be a source of embarrassment and concern to the predisposed patient. These patients frequently maintain their weight once it is gained in spite of very genuine and strenuous efforts to lose it. I fear that the long-term results of this drug-induced obesity may prove to be one of the most harmful sequelæ of chlorpromazine and reserpine therapy, and I would suggest that further investigation of this problem would be wise.

The advantages of "Meratran" and "Ritalin" over the amphetamines have already been stressed (Morgan, 1956*b*).

In passing, it might be mentioned that I have used reserpine and "Ritalin" together to treat depression, but this combination has not proved encouraging in my hands except in two cases of schizophrenia with depressive features. For those who are interested, I would draw attention to an article published recently by Mielke (1956) from the Burgholzi Clinic in Zurich, where endogenous depression has been treated with reserpine.

Reports of Cases.

The following seven case histories are typical of the many in which the treatment already described has been given.

CASE I.—The patient is a woman, now aged seventy-seven years; her blood pressure is 160 millimetres of mercury, systolic, and 90, diastolic. She was admitted to a mental hospital under my care in 1949, the first signs of depression having appeared a year earlier. The patient was deaf, and at this time extremely agitated and depressed. She feared that criminals were conspiring to kill her and she could be persuaded to eat only with the utmost difficulty. She was very thin, and showed considerable evidence of arteriosclerosis with early myocardial degeneration. Her condition deteriorated, and she became increasingly depressed, mute and inaccessible. In spite of the risks involved, she was given electrotherapy and made a good recovery, and fourteen months after her admission she left hospital to live with a niece in the country. With some depressive phases she remained comparatively well until July, 1955, when she was readmitted to this hospital, once more acutely depressed. She said that she was too wicked to live, had delusions of unworthiness, and believed that she had an incurable disease. Her physical health was precarious, but with "Brevedil E" and thiopentone she was given electrotherapy and her condition improved. It was found that it was necessary to give her two or three electroshock treatments in this manner every four to six weeks to maintain her in good health. As she grew older, this form of treatment became an increasing hazard and involved a considerable risk. In December, 1955, she was given "Largactil", 100 milligrammes twice a day, but even so required electrotherapy occasionally. In April, 1955, "Ritalin", 20 milligrammes twice a day, was added to this regimen, and she has remained well since; she is bright, cheerful and cooperative, and worked in the occupational therapy department until her failing eyesight made this impossible. She has had no electrotherapy for over eight months.

Drug therapy has thus proved a tremendous help for this particular woman, because of the increasing risks involved in administering electrotherapy to a patient so advanced in age.

CASE II.—The patient was a woman, aged sixty-seven years, whose blood pressure was 160 millimetres of mercury, systolic, and 105 millimetres, diastolic. She was admitted to hospital extremely agitated and depressed. She said that she was very wicked, and that her son and his children had all been killed. She had become acutely depressed after the death of her husband six months before, and was now refusing food. She was given chlorpromazine, 200 milligrammes twice a day by injection, with "Ritalin", 20 milligrammes three times a day and parenteral vitamin therapy. She made a splendid recovery, proceeding on leave seven months after her admission to hospital.

CASE III.—The patient was a woman, aged forty-three years. Her blood pressure was 120 millimetres of mercury, systolic, and 72, diastolic. She was admitted to hospital in March, 1956, depressed, uninterested, dirty and neglected. She had suffered from bouts of depression during the past five years, for which she had been treated with electrotherapy by a private psychiatrist. On her admission to hospital she had some unsystematized paranoid ideas concerning her neighbours. She was treated at first with "Meratran", five milligrammes twice a day, but showed no improvement. In April the drug was changed to "Ritalin", 20 milligrammes twice a day, again with no improvement. To this regimen was added chlorpromazine in a daily dosage of 200 milligrammes, and she made a continuous and uninterrupted improvement, proceeding on leave seven months after her admission to hospital.

CASE IV.—The patient was a woman, aged seventy-eight years. Her blood pressure was 200 millimetres of mercury, systolic, and 112, diastolic. She was admitted to hospital, acutely depressed, for the third time since 1944. On the two previous occasions she had been treated with electrotherapy. On her last admission to hospital she was extremely depressed, anergic, thin and debilitated. She stated that she was affected by the "black-fly disease" which prevented her from sleeping, and she wished she could die. She was treated with "Largactil", 100 milligrammes twice a day, and "Ritalin", 20 milligrammes three times a day. Over a period of five months she gained considerable weight. On leaving hospital she was very well, and she has remained so since.

CASE V.—The patient was a woman, aged forty-four years. Her blood pressure was 125 millimetres of mercury, systolic, and 80 millimetres, diastolic. She was admitted to hospital for the first time in 1953, when she was miserable, depressed and self-absorbed. She said that people were spying on her, and she had attempted to commit suicide by cutting her wrists. The paranoid content of her delusions was based on her war experiences in Poland prior to coming to Australia in 1949. She was given electrotherapy and improved; but in six weeks she relapsed and was again given electrotherapy, when her husband stated that he thought her memory was impaired. She proceeded on leave two months later, and whilst away from the hospital was treated by a private psychiatrist with electrotherapy for a recurrence of the depression. She was discharged, on this doctor's recommendation, nine months later.

She was admitted to hospital again in October, 1955, tearful, agitated and depressed. She believed that her husband was poisoning her, and she had once more been contemplating suicide. Again she was given electrotherapy and went on leave six weeks after her admission. Three months later she returned to hospital, acutely depressed once more. She was now treated with "Largactil", 200 milligrammes, and "Meratran", 10 milligrammes, twice a day, and improved to such an extent that she was permitted to proceed on leave again six months later.

Four months after this she again returned to the hospital, acutely depressed, and it was ascertained that she had not been taking her tablets as she had felt so well.

She was treated with "Largactil", and on this occasion, "Ritalin", 20 milligrammes twice a day, and was kept in hospital continuously on treatment for three months to ensure a stabilized recovery. She has now been on leave from the hospital for nearly six months, and has been advised to continue taking chlorpromazine, 100 milligrammes twice a day, and "Ritalin", 10 milligrammes twice a day, for at least another twelve months.

CASE VI.—The patient was a woman, aged thirty-six years, married, with three children. Her blood pressure was 152 millimetres of mercury, systolic, and 100 millimetres, diastolic. She was admitted to hospital acutely depressed and mute, having made two simultaneous attempts at suicide—one by taking an overdose of a sedative mixture, and the other by shooting herself; but her aim was poor and she was not successful. There was a long, involved history of financial stress and living under most difficult conditions on a small farm of the outskirts of Sydney. Her ex-serviceman husband had been drinking to excess and had been admitted to hospital. She was left to cope with the children and the farm. Her depression had been gradually increasing since the loss of a child a birth, seven months prior to her admission to hospital. She had not had any respite from work for the past four years.

She was treated with "Largactil", 300 milligrammes twice a day, and "Ritalin", 20 milligrammes twice a day. Her mental health improved to the extent that she became accessible to psychotherapy. At the same time, the social worker was able to improve her home conditions, and she went on leave three months after her admission to hospital. She has been home over six months and has remained well.

CASE VII.—The patient was a woman, aged sixty-five years. Her blood pressure was 98 millimetres of mercury, systolic, and 74 millimetres, diastolic. She was admitted to hospital acutely depressed and refusing food. She had to be spoon-fed and took no interest in herself or her surroundings, being utterly absorbed with her hyperchondriacal ideas. She was slow in her movements and retarded in her thinking, and believed that she could never get well. She was thin and emaciated, and showed considerable evidence of avitaminosis.

She was so acutely depressed that it was decided to give her electrotherapy, with thiopentone, and "Brevedil E". At the same time she was given "Meratran". After three electroconvulsive treatments she improved to such an extent that this form of therapy was replaced with "Largactil", 100 milligrammes in the morning and 200 milligrammes at night. Seven weeks after her admission to hospital she proceeded on leave, taking both "Largactil" and "Ritalin". She has now been home for eight months and remains well.

Comment.

From the foregoing case histories it will be seen that considerable success has been attained in the treatment of acute endogenous depression with chlorpromazine, combined with either "Ritalin" or "Meratran". There have been virtually no complications with this mode of therapy, and one of the most impressive features has been the manner in which patients who were previously prone to frequent relapses have maintained a relatively stable affect, both in the hospital and away from it, by taking maintenance doses of the drugs. How long this therapy should be continued is more than I can say at present, but I believe that it should be from one to two years.

A remarkably prophetic statement was made a few years ago (Alexander, 1953): "It is, however, definitely within the bounds of possibility that shock treatment may someday be replaced by a variety of 'pills'—one of their ingredients would have to be a powerful cholinergic (parasympathomimetic) substance, probably with marked sudorific side-effects." This is precisely what has happened.

Now the question may be asked, how far has the exhibition of chlorpromazine and "Ritalin" replaced the need for electrotherapy? I myself believe that the two forms of treatment are complementary. I still consider that electrotherapy is the quickest and most reliable method of treating psychotic depression; but drug therapy, if intelligently used, is almost as efficacious—its most serious disadvantage being that it takes longer to bring about an amelioration of the patients' symptoms than does electrotherapy. Also, some patients, when admitted to a mental hospital, are in such a shockingly debilitated condition that it becomes a matter of life and death to restore their internal chemical *milieu* to normal as rapidly as possible. To attain this end, it is most important to have the patients' full cooperation, and in my experience this cooperation may be best obtained with electrotherapy.

However, when the urgency is not paramount, then the use of chlorpromazine and "Ritalin" has many advantages. The patients do not fear taking tablets, whereas many are afraid of electrotherapy, even when it is given in combination with sedatives and muscle relaxants. Also, it is comforting to have an alternative to electrotherapy when one is treating an acutely depressed patient who has an advanced physical illness such as pulmonary tuberculosis or increasingly severe degenerative myocardial disease. Chlorpromazine also enables the patient with acutely agitated depression to sleep satisfactorily without the need to prescribe so much nightly sedation that he remains chemically confused the following day.

Of course, a judicious mixture of the two modalities of treatment is also advantageous, as will be noted from the case histories. It may well be that the patient can be started on the drugs, and at the same time receive two or three electroconvulsive treatments to bring about a more speedy clinical remission, and then continue with drug therapy alone; thus the advantages of both therapies will be combined. Decisions such as these will rest, of course, with the individual psychiatrist and the needs of a particular patient.

In any case, it is only by experimenting with the various therapeutic tools which we now have at our disposal that any real progress can be made in establishing the proper criteria for the exhibition of a particular form of therapy in a particular disease. It is in this spirit than this paper is presented.

Acknowledgements.

Once more I wish to acknowledge the ever-ready advice and constant encouragement I have received from Dr. Eric T. Hilliard, Medical Superintendent, Mental Hospital, Parramatta. This paper is published with the permission of Dr. Donald S. Fraser, Inspector-General of the Insane, New South Wales Department of Public Health, Division of Mental Hygiene.

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OUTLINE OF EARLY RADIOIODINE UPTAKE TESTS FOR THE ASSAY OF THYROID FUNCTION.

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A BRIEF description is given here of the principles underlying the assay of thyroid function with radioiodine when this is measured *in vivo* in the early stages after administration of a tracer dose. A more detailed mathematical treatment has already been published (Oddie *et alii*, 1955*a*), together with a full description of practical test methods (Oddie *et alii*, 1955*b*) and some results (Oddie *et alii*, 1955*c*).

The diagnostic value of radioiodine tests is now well established (Rundle, 1956), and with proper care these can be made as early as thirty minutes after injection (Berson *et alii*, 1952), although a longer time (Oddie *et alii*, 1955*b*) is preferable with possibly hypothyroid patients.

Metabolism of Tracer Dose.

Let us consider first the early movements of a tracer dose of which both the radioactive and chemical iodide contents are so low that there is no disturbance of the patient's iodide metabolism.

For reliable early tests an accurately measured dose should be injected intravenously to establish a definite "zero" time. The residual radioiodine (about 2% to 6%) that is left behind in the injection apparatus should also be measured and deducted, to find the net dose.

Zero time is half-way through the injection, which normally takes about ten to twenty seconds. After that the radioiodide moves up the arm veins to the heart, to the lungs, back to the heart, and then out through the arterial system; so the process of initial mixing with the circulating plasma should be rapid. Thereafter the radioiodide continues to diffuse into the intercellular and intracellular fluids; it may accumulate to a minor extent in the saliva, the liver and the gastric mucosa, so that the amount of radioiodide per unit volume of plasma decreases slowly, quite apart from any decrease resulting from removal of iodide by the thyroid gland or the kidneys. In other words, the apparent volume V of the total "iodide space" increases with the time after injection. Figure I shows how the average experimental curve for V, deduced (Oddie *et alii*, 1955*a*) from results published by several groups of authors, rises slowly to a maximum saturation value as the diffusion of radioiodide progresses.

Concurrently with the above-mentioned diffusion process, radioiodide is removed from the plasma by the thyroid gland and by the kidneys at rates representing the clearance (Myant *et alii*, 1949) of iodide from a fixed volume of plasma each minute. If the iodide space had a constant volume V, these combined clearances would result in the removal of a constant percentage of the circulating iodide each minute, the amount remaining being given by a simple exponential term of the form e^{-kt}. In practice, however, as diffusion progresses there is less radioiodide per millilitre of plasma, and therefore a decreasing percentage rate of removal results from thyroid and renal clearance. Such a decreasing rate can be allowed for by introducing a factor ϕ so that $e^{-k\phi t}$ represents the proportion of the injected dose remaining in the plasma iodide space t minutes after injection.

Values of ϕ can be deduced (Oddie *et alii*, 1955*a*) from the curve for V, and also independently from several observations of the radioiodine accumulated by the thyroid gland or excreted in the urine. Figure II shows how the average curve for ϕ decreases asymptotically to a minimum value, corresponding to the asymptotic rise in the volume V.

In the absence of any antithyroid medication, the above-mentioned processes describe reasonably well the early metabolism of a tracer dose, before any radioiodine leaves the thyroid gland in organic form. The basic quantities to be considered are as follows (Oddie *et alii*, 1955*a*).

The fraction G of the injected dose accumulated in the thyroid gland at time t minutes after "zero" time:

$$G=(1-e^{-k\phi t})k_1/k \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

The fraction E of the dose excreted in the urine up to time t:

$$E=(1-e^{-k\phi t})k_2/k \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (2)$$

The fraction P of the dose remaining in the plasma iodide space at time t:

$$P=e^{-k\phi t} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (3)$$

The rate factor k_1 minute^{-1} represents the fractional rate of removal of radioiodide by the thyroid gland, k_2 minute^{-1} is the corresponding rate for the kidneys, and k is the total rate, being the sum of k_1 and k_2. In other words, the thyroid gland removes 100 $k_1\phi$ *per centum* of the total plasma radioiodide each minute, and the kidneys 100 $k_2\phi$ *per centum*, while

$$k=k_1+k_2 \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (4)$$

Observations with an External Counter.

Now consider what is observed by a collimated Geiger or scintillation counter aimed externally at the thyroid gland of a patient who has been given radioiodine.

The lead collimator of the counting apparatus will allow a certain umbral region of tissue to be "viewed" by all parts of the detector (crystal or sensitive region of the Geiger-tube), and there will be a further penumbral region viewed by only some parts of the detector. Figure III illustrates these regions for the long conical collimator previously described (Oddie *et alii*, 1955*a*); of course, collimators of different design will view regions of tissue of different shape and size.

If, as is usual, only γ rays are allowed to enter the counter, they will be received from the following four sources: (*a*) radioiodine in the thyroid gland; (*b*) radioiodine in that part of the iodide space in the umbral and penumbral regions of tissue; (*c*) radioiodine in adjacent parts of the iodide space outside the umbral and penumbral regions, emitting radiation that can be scattered into the detector; (*d*) cosmic rays and other background sources, for which the usual allowance can be made.

[1] This work was done during the tenure of a Fulbright Fellowship at the University of Arkansas Medical Center, Little Rock, Arkansas, and at the Bowman Gray School of Medicine, Winston-Salem, North Carolina.

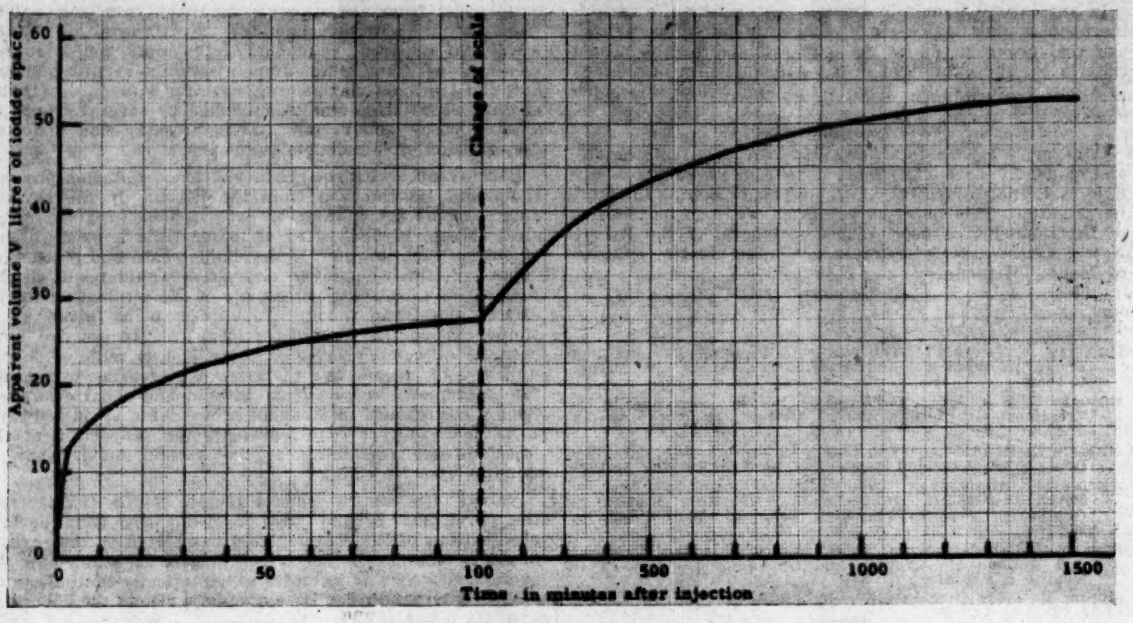

FIGURE I.
Variation of apparent iodide space with time after injection in the average patient.

For the simplest theoretical case, with an athyroid patient with no renal function ($k_1 = k_2 = 0$), all the radioiodine remains in the iodide space. However, the amount of circulating radioiodide that is viewed by the counter is not necessarily a constant proportion of the total in the whole iodide space, because it is likely that diffusion takes place at different rates in the different regions of tissue. In fact, with the collimated counter described (Oddie *et alii*, 1955*a*), the fraction Q of the total radioiodide[1] observed by the crystal decreases sharply from an initial value of 0·096 at zero time, tending to an asymptotic value of 0·037, as shown in the curve in Figure IV.

In the more general case in which there is thyroid and renal activity as well, it is evident that the radioactive content of the whole iodide space is reduced by the factor e^{-kvt}, as given by equation (3). So the fraction observed by the counter is made up of G from the thyroid gland itself, and Qe^{-kvt} from the non-thyroid tissue viewed—that is, items (*b*) and (*c*) above. If N is the total fraction of the dose observed in the neck,

$$N = Qe^{-kvt} + G \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (5)$$

[1] In the full mathematical treatment (Oddie *et alii*, 1955*a*, *b*, *c*) this fraction Q was written N_0V_0/V.

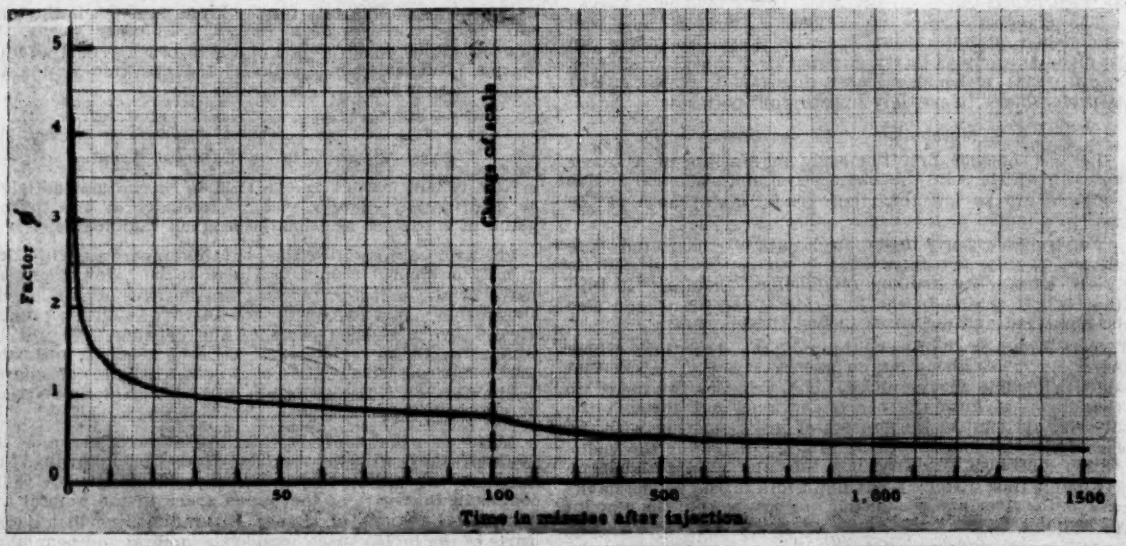

FIGURE II.
Variation of factor ϕ with time after injection in the average patient.

Equation (5) shows how the observed fractional uptake N in the neck depends not only on the activity G in the thyroid gland itself, but also on the circulating iodide within view. The latter becomes important for borderline hypothyroid cases in which the measurements are made twenty-four hours after injection, and for nearly all cases in which observations are attempted within an hour or so after injection. It should be remembered that the values for Q given in Figure IV apply to a narrow collimator; Q may be three times as large for a commonly used arrangement of a cylindrical Geiger counter placed transversely to the neck in an open lead-box collimator. Even the shoulders of the patient shown in Figure III would be in the field of view of such a detector. Sometimes a reading with the counter placed over the patient's thigh is used to correct for the non-thyroidal part of N; but this is unlikely to be accurate when wide collimation is used.

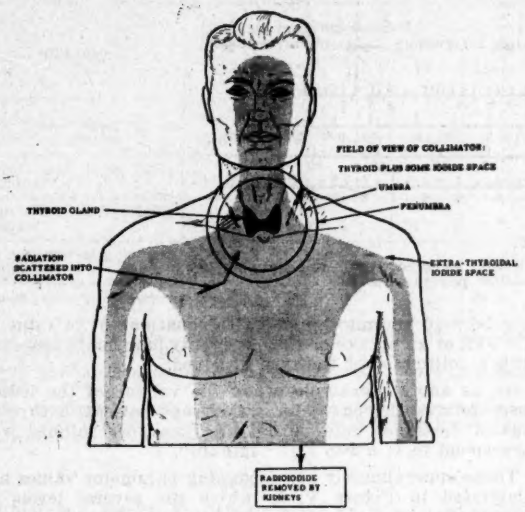

FIGURE III.
Diagram showing the field of view of a counter.

Routine Measurements for Assay of Thyroid Status.

The counting apparatus should be calibrated by means of suitable phantoms, so that due allowance can be made for absorption and backscattering of the observed γ rays; once this is done, N can be found from the ratio of the counts over the thyroid gland to the counts with a known source of radioiodine.

Similarly, the fraction E of the dose in the urine can be found by routine counting methods, and the rate factors k_1 and k_2 follow from equations (1), (2), (4) and (5) by applying the known average values (Oddie *et alii*, 1955*a*) for Q and ϕ. These calculations can be made (Oddie *et alii*, 1955*b*) for a few selected times t after injection, so that charts can be prepared enabling k_1 and k_2 to be read off directly; then for routine tests no further calculation of k_1 or k_2 is necessary.

For hyperthyroid or "high normal" patients with rather high k_1 rate factors, a convenient time of observation is $t = 60$ minutes after injection; thus the counting rate over the neck is observed for ten minutes from $t = 55$ to 65 minutes, the urine is collected and assayed to find E, and k_1 and k_2 are found from the charts. With such cases there is no advantage in prolonging the time of test, because only a few hours are needed for practically all the tracer dose to be accumulated in the thyroid gland and in the urine; when this happens, only the ratio k_1/k_2 can be found with any accuracy, and k_1 itself becomes uncertain. Moreover, a very active gland may lose radioiodide as hormone if the measurements are delayed.

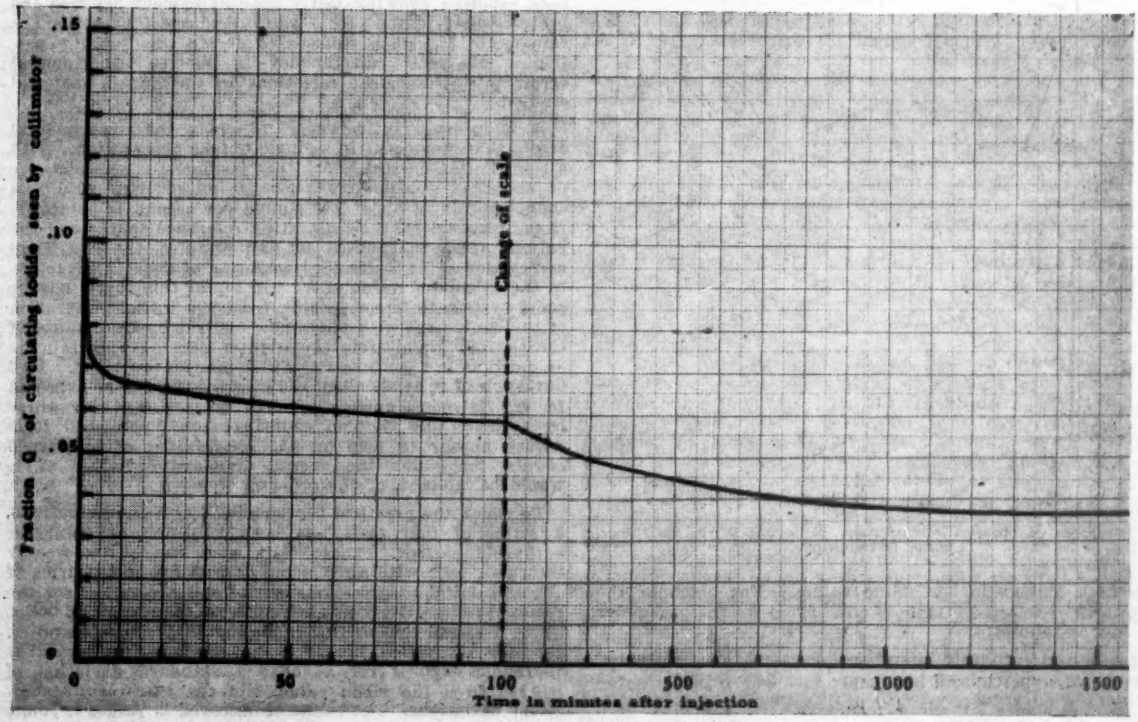

FIGURE IV.
Time variation of fraction Q of circulating iodide observed by a particular collimated counter.

Low normal or hypothyroid patients, on the other hand, are best studied at longer times t, because at one hour there is insufficient rise of radioactivity in the thyroid gland. Often a statistically significant rise in the counting rate can be observed at $t = 4$ hours, while with very hypothyroid, myxœdematous patients the test may be repeated in twenty-four hours.

Corresponding borderline values can also be derived for other parameters, when certain characteristics are assumed for a "standard" patient.

For example, while the renal rate factor k_2 has little significance as far as thyroid function is concerned, it does affect the observed twenty-four hour percentage uptake; for $k_1 = 3{\cdot}85 \times 10^{-3}$ minute^{-1}, the average renal rate

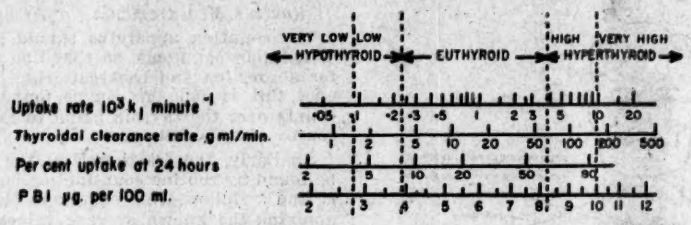

FIGURE V.
Chart showing diagnostic borderline values selected, and approximate corresponding values of other parameters.

Diagnostic Borderline Values for Rate Factors and Other Parameters.

All tests in which radioiodine is used for the assay of thyroid status rest on the assumption that the numerical result can be interpreted, at least approximately, in terms

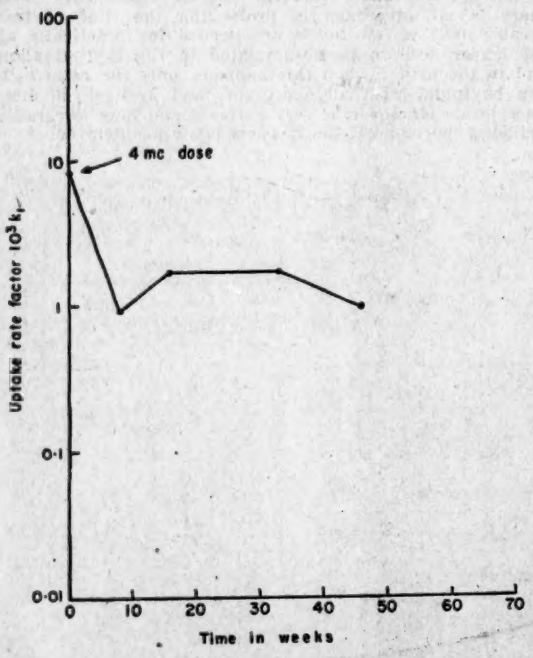

FIGURE VI.
Progressive observations of rate factor k_1 on a patient given I^{131} therapy.

of some diagnostic borderline values. For example, the borderlines selected (Oddie *et alii*, 1955c) for the parameter k_1 are as follows:

hypothyroid/euthyroid boundary; $k_1 = 0{\cdot}23 \times 10^{-3}$ minute^{-1}
euthyroid/hyperthyroid boundary; $k_1 = 3{\cdot}85 \times 10^{-3}$ minute^{-1}

In the choice of these boundaries, weight has been given to data published from several clinics, amongst which there is fair agreement at least as to the upper boundary.

$k_2 = 2{\cdot}6 \times 10^{-3}$ minute^{-1} gives, with equation (5), a value of $N = 0{\cdot}62$, or an uptake of 62% at twenty-four hours observed with a collimator of the type specified.

Or, as another example, when the volume of the iodide space follows the curve for an average patient, a thyroid plasma clearance rate of 63 millilitres per minute will correspond to $k_1 = 3{\cdot}85 \times 10^{-3}$ minute^{-1}.

These approximately corresponding parameter values are illustrated in Figure V, in which the several levels of thyroid activity are indicated by interrupted vertical lines.

Accuracy to be Expected.

In an earlier paper (Oddie *et alii*, 1955c), results have been reported showing fairly good agreement between the protein-bound iodine (PBI) values and the I^{131} test for the rate factor k_1. It is difficult to decide whether any particular diagnostic discrepancy is due to experimental errors or to biological variations in the human material studied.

It is informative, however, to study the experimental errors that may occur in a single uptake observation. With a scintillation crystal 1·75 inches in diameter at a distance of about 28 centimetres from 10 microcuries of I^{131}, a counting rate of about 150 counts per second is obtained; if the tracer dose, the calibrating reference source and the patient are each counted for ten minutes, the statistical errors alone give a standard deviation of about 2·5% to 3% in the calculated value of k_1. On top of this there may be some systematic error arising from the initial calibration of the equipment with phantoms, and the mean distance of the thyroid gland from the counter may be uncertain by as much as ± 1 centimetre. Altogether an overall standard deviation of $\pm 5\%$ is about the best accuracy to be expected for k_1. It seems unwise to make the accuracy any worse by reducing the time of counting; some published techniques appear to rely on the observation of only 2000 counts, for which the overall standard deviation of k_1 would be, at best, of the order of $\pm 2\%$.

To check the practical reproducibility of k_1 observations, a series of four tests has been run on one volunteer euthyroid patient. These tests were run at two-weekly intervals, each with an injected dose of five microcuries of I^{131}, and suitable corrections were applied to allow for the residual radioactivity left behind from the preceding doses. Table I shows the results, including PBI values found on the day on which the I^{131} tests were performed. The individual figures for k_1 have a standard deviation of $\pm 12\%$ from the mean value, and the PBI results show wider variations. The range of observed k_1 values is found to extend over a width equal to 10% of the linear distance (Figure V) between the hypothyroid/euthyroid and euthyroid/hyperthyroid boundaries; similarly the range

for the twenty-four hour percentage uptake covers 9%, and the PBI range covers 60% of this distance.

With this particular subject the PBI tests indicated an average level of thyroid activity somewhat lower than the I^{131} tests showed.

TABLE I.

Summary of Results of I^{131} and PBI Observations Repeated at Two-weekly Intervals on the One Euthyroid Subject.

Quantity.	Test Results.				
	I.	II.	III.	IV.[1]	Mean.
Neck tissue factor Q at time $t=2$ minutes ..	0·073	0·081	0·064	0·082	0·075[2]
Thyroid rate factor 10^2k_1 minute^{-1}	1·06	1·22	1·08	1·43	1·20
Renal rate factor 10^2k_2 minute^{-1}	2·3	2·2	3·6	3·6	2·9
PBI microgrammes per 100 millilitres[3]	3·8	4·9	2·8	3·2	3·7
24-hour percentage uptake	27·7	33·8	28·7	28·1	29·6

[1] No medication was given except twelve hours prior to test IV, when 300 microgrammes of stable iodide were ingested.

[2] This figure may be compared with the value 0·072 obtained for the average patient.

[3] PBI determinations were made during a period of alteration of technique and change in personnel. The usual range of reproducibility is less than one microgramme per 100 millilitres.

Discussion.

When the limits of experimental accuracy, estimated above, are considered in conjunction with the diagnostic results on large series of patients (Oddie *et alii*, 1955c), it seems certain that only badly overlapping results can be expected for borderline groups of patients unless a good experimental technique is maintained. With a good technique, including sufficient statistical accuracy in the counts observed, early I^{131} tests can be a reliable index of thyroid status.

Moreover, with the elimination of errors arising from radioiodide in the non-thyroid neck tissues, I^{131} methods can replace basal metabolic rate observations over the whole range from hyperthyroid down to athyroid patients. Radioiodine measurements, unlike the basal metabolic rate results, are unaffected by the emotional state of the patient at the time of test. However, the basal metabolic rate estimation still retains its usefulness in finding the metabolic status of patients under the influence of thyroid-affecting medications, which usually interfere with the I^{131} results.

A further application for the use of precise diagnostic I^{131} tests is in the follow-up investigation of patients who have been treated therapeutically with radioiodine.

Figure VI shows, on a logarithmic scale, the values of the thyroid rate factor k_1 observed in a hyperthyroid patient just before a therapeutic drink of four millicuries of radioiodine, and also eight, sixteen and thirty-three weeks later. This patient began with $k_1 = 8{\cdot}2 \times 10^{-2}$ minute^{-1}, which dropped two months later to $0{\cdot}9 \times 10^{-2}$ and then remained between this and $1{\cdot}6 \times 10^{-2}$. Both of the two last-mentioned limits are in the euthyroid range.

Summary.

An outline is given of methods for the assay of thyroid status, by the use of the uptake of radioiodine observed at early times after injection. The experimental accuracy that can be expected from such tests is discussed, and results are given for repeated measurements on the one subject.

Acknowledgements.

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THE ACTION OF LEUCHÆMIC CELLS ON NEUTRAL FAT.

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THE excessive growth of leuchæmic cells suggests that they have access to nutriment which is unavailable to normal cells. In the following essay, the writer concludes that leuchæmic cells *in situ* have an abnormal capacity to utilize neutral fat as an auxiliary foodstuff.

The approach to this conclusion begins with a well-known observation—namely, the disappearance of marrow fat in myeloid leuchæmia and its replacement by an overgrowth of leucocytes (Dietz and Steinberg, 1951). Hitherto the fate of the marrow fat which disappears in leuchæmia has not received close attention.

Marrow fat, however, is of great biological significance, for it is a reserve store of chemical energy, accumulating as the subject develops from childhood towards adult life. Marrow fat is a foodstuff, and when it disappears the logical course is to inquire what has happened to it. The disappearance of marrow fat in myeloid leuchæmia could conceivably be due to one or more of the processes which will now be discussed.

1. Transfer of marrow fat into the blood-stream by the subject's normal regulatory processes of fat mobilization. This interpretation implies that the subject's regulators of fat metabolism are conveniently making room for a fatal overgrowth of leuchæmic cells by eliminating adipose tissue from the bone marrow. Such a view is contrary to the general opinion that leuchæmia is a disorder which occurs in opposition to the regulatory functions of the organisms as a whole.

2. Mechanical displacement of marrow fat into the blood-stream by an unexplained overgrowth of leucocytes in the bone marrow. This interpretation assumes that leucocyte multiplication forces marrow fat out of the bone marrow by mechanical pressure. Equally hypothetical would be the assumption that replacement of blood cells by adipose tissue, in the bone marrow of healthy adolescents, was due to mechanical pressure on blood cells by accumulating marrow fat. Neither assumption is supported by experimental evidence. Moreover, in other parts of the body mechanical pressure does not cause the disappearance of adipose tissue, as patients with obesity are fully aware. Biochemical rather than mechanical causes are generally held to be responsible for increase or decrease of adipose tissue.

3. Oxidative breakdown of neutral fat in the bone marrow, and assimilation of the products of marrow fat oxidation by leuchæmic cells. This process is here taken to be the metabolic abnormality responsible for the disappearance of marrow fat in myeloid leuchæmia. The writer regards malignant growth, including that of leuchæmia, as the outcome of an abnormal capacity of

cancer cells to oxidize neutral fat of the organism as a whole, and to obtain thereby an auxiliary supply of nutriment which is unavailable to normal cells.

Neutral fat, including marrow fat, is not directly available for the nutrition of normal cells in man and other animals. Bloor (1943) wrote as follows:

> Stored fat is not directly used, either near its storage place or elsewhere, but is first carried to the liver, altered, and then redistributed for use, presumably as phospholipid or acetone bodies.

Peters and Van Slyke (1946) made the following statement:

> While fats can be used directly for storage in the depots, they cannot gain access to tissue cells . . . . The liver appears to select and combine the proper constituents to make phospholipids—or at least phosphatides—suitable for other cells.

Neutral fat reaching the liver is normally metabolized into phospholipid at a rate which prevents excessive accumulation of neutral fat in the liver. If dietetic or other factors lead to an excessive and long-continued accumulation of neutral fat in the liver, as in kwashiokor, primary carcinoma of the liver becomes more frequent (Brock and Autret, 1952).

Other facts suggest that accumulation of neutral fat at certain sites favours carcinogenesis. The administration of ACTH, which tends to increase the fat content of various tissues (Li, 1948), has been found to increase the incidence of leuchæmia in mice. Silberberg (1955) gave adrenocorticotrophin to male mice of strain C57 BL over a period of five months, and noted a sevenfold to tenfold increase in the incidence of lymphoma (lymphoid leuchæmia and lymphosarcoma). The highest susceptibility was observed in animals in which the hormone treatment was begun during the period of growth.

While certain tissues where neutral fat is accumulating, such as the bone marrow of adolescents, are apparently favourable sites for carcinogenesis, the development of malignant growth depletes local reserves of fat. This is most evident in the bone marrow in cases or leuchæmia, but it has also been observed in early stages of experimental carcinogenesis. Wicks and Suntzeff (1942) have reported the following significant findings:

> During an investigation of possible alterations in the lipids of the epidermis of mice treated topically with a benzene solution of methylcholanthrene, one change stood out conspicuously and consistently. This was the marked and sudden reduction in the total epidermal lipid material. Five days after even a single application of the carcinogen, the total fatty substance of the epidermis fell to less than 40 per cent of that at the normal level. This effect was due to the carcinogen alone and not to the solvent, for values of the benzene-treated controls agreed well with those of the untreated skins.

To turn from carcinogenesis to the histopathology of malignant tumours, lack of adipose tissue is evident, even where connective tissue is abundant. In the cancerous connective tissue of a sarcoma, and in the connective tissue stroma of malignant epithelial tissue, the presence of normal fat cells is rarely reported.

The writer's conclusion that cancer cells oxidize breakdown products of neutral fat is in accordance with the low respiratory quotient of cancer tissue (Greenstein, 1947). However, it is not implied that cancer cells have special nutritional requirements, or that the nutrition of cancer cells always exceeds that of corresponding normal cells. On the contrary, the "dormancy" of some cancer cells for long periods of time (Hadfield, 1954) indicates that in some circumstances the nutrition of cancer cells *in situ* does not exceed that of corresponding normal cells, so that malignant growth of cancer cells does not then occur.

The dependence of malignant growth on circumstances in which cancer cells have a nutritional advantage over corresponding normal cells is also indicated by tissue culture observations. *In vitro*, tissue culture conditions provide the same nutrition for normal and cancer cells, and under such conditions there is no general distinction of growth between normal and cancer cells. "There is no essential difference between the growth of malignant tumour cells and normal tissue cells in cultures." (Fischer, 1946.) Tissue culture observations thus support the writer's view that cancer cells *in situ*, in circumstances in which their growth exceeds that of corresponding normal cells, have access to nutriment which is unavailable to the normal cells.

As has already been mentioned, neutral fat is unavailable to normal cells *in situ*, and it is this nutriment which disappears at sites of developing malignant growth, especially the bone marrow in cases of myeloid leuchæmia. If leuchæmic and other cancer cells do actually assimilate breakdown products of the oxidation of neutral fat, the oxidative process must be abnormal. Neutral fat *in situ* is not subject to normal oxidative processes. Neutral fat is the forbidden fruit of the animal body—a food reserve which is normally unoxidizable, and must be metabolized into phospholipid or other nutriment before it can be consumed by normal cells.

The abnormal process by which neutral fat seems to be broken down, in leuchæmia and in other forms of malignant growth, is apparently autoxidation. The most outstanding known cause of human leuchæmia—namely irradiation (March, 1950; Amano, 1952)—is a potent initiator of autoxidation of neutral fat *in vitro* (Hannan, 1955).

Among certain primitive unicellular organisms, such as bacteria which cause oxidative rancidity in milk, autoxidation of neutral fat is a normal process. Colonies of these bacteria can be distinguished by the rose-red colour they assume when a 0·5% aqueous solution of dimethyl-p-phenylenediamine hydrochloride is poured over the culture plate (Chalmers, 1945).

In the higher animals, however, autoxidation of neutral fat is not a normal process, and it does not necessarily involve the hydrolytic process catalysed by lipase. Autoxidation is a breakdown process of oxygen absorption, in which free radicals and other unstable chemical entities are formed (Farmer, 1942) and catalyse further uptake of oxygen (Davies, 1936).

Once started by some initial cause, physical or chemical, autoxidation continues indefinitely as a self-perpetuating process, the chain reactions of which involve the continued formation of free radicals and peroxides (Waters, 1948). "These and other highly reactive entities can be produced freely by ionizing radiations". (Hannan and Shepherd, 1954.) After a preliminary induction period, small amounts of the free radicals, peroxides and other highly reactive entities continue the oxidative process autocatalytically, if conditions permit.

There is a striking parallel between the induction period of fat autoxidation *in vitro* and the latent induction period of experimental carcinogenesis. In neutral fat exposed to oxygen and metal ions or other accelerators of autoxidation, "the rapid progress of the reaction is preceded by a period of relative inaction, known as the induction period, during which the primary reaction of chain formation is proceeding at the same maximum rate as later, but the chains are being broken as fast, or almost as fast, as they are started" (Mattill, 1947).

With carcinogenesis, the induction period of malignant growth ranges from a few weeks for experimental tumours of mice to several years for human occupational tumours. The writer predicts that adequate examination of fresh biopsy specimens from susceptible animals exposed to carcinogenic agents, will show typical features of the induction period of fat autoxidation during the latent induction period of malignant growth. It is also predicted that in biopsy specimens of bone marrow from human subjects of leuchæmia, the chain reactions of fat autoxidation will be detected.

Already peroxides have been found in neutral fat of living mice irradiated with X rays (Bacq, Burg, Chevallier and Heusghem, 1951). Using whole mice who were given a lethal dose of X rays, Horgan and Philpot (1954) made subsequent cell extracts with n-butanol and found peroxide present. Duboulez, Dumas and Vigne (1950), working

with albino rats, found peroxides present in the skin after burns, as well as after irradiation *in vivo* with X rays. Peroxides were not found in the skin of control animals.

From the foregoing data, the following provisional picture of the characteristic cell response to carcinogens can be formed.

Owing to extrinsic or intrinsic carcinogenic agents, autoxidation of neutral fat is initiated at one or more sites of the animal body, thus creating an abnormal metabolic situation. Cells which adapt themselves to the abnormal situation and participate in the abnormal process of neutral fat autoxidation are cancer cells.

Cancer cells, like certain microorganisms, induce autoxidation in surrounding neutral fat and have an abnormal capacity to assimilate breakdown products of this abnormal oxidative process. The report of a polarographic study by Carruthers and Suntzeff (1949) states that the fat of induced epidermal cancer tissue of mice is qualitatively different from the fat of normal mouse epidermis.

Fat autoxidation, which causes rancidity of neutral fat *in vitro*, may contribute to the cachexia associated so often with malignant growth. The toxic effects of feeding animals with fat which has become rancid through autoxidation are well known (Barnes, Clausen, Rusoff, Hanson, Swendseid and Burr, 1949).

Cancer cells can grow autonomously because they derive from fat autoxidation an auxiliary nutritive supply of chemical energy, which gives them powers of growth beyond those of corresponding normal cells. Cancer cells are "outlaw" cells because they take part in destruction of forbidden food reserves of the body—the neutral fat of blood, lymph and adipose tissue.

With the application of more refined methods of chemical analysis to examination of bone marrow and lymph glands from subjects of leuchæmia, it will be possible to detect therein the unstable peroxides of fat autoxidation, and to trace the careers of free radicals in abnormal chain reactions. Thereby, the long-sought secret of malignant growth may be found, and the problem of leuchæmia solved.

With this picture in view, the question of controlling leuchæmic growth assumes a more definite outline. In so far as leuchæmic cells differ from normal leucocytes, in living on stored or circulating neutral fat as an auxiliary foodstuff, the object of one method of treatment is to transmit growth-controlling compounds, in a vehicle of neutral fat, direct to the bone marrow and lymph glands without passing through the liver.

To this end, therapeutic substances dissolved in neutral carrier fat are given by the mouth, together with sodium cetyl sulphate. Lipolysis of the carrier fat in the intestine is thus prevented, since unhydrolysed fat, protected from lipase by sodium cetyl sulphate, "passes directly as such by the lacteal-lymphatic system and thence to the fat depots" (Hilditch, 1949). By this route, which by-passes the liver (Frazer, 1943), the carrier fat avoids early transformation into phospholipid, and the contained therapeutic substances are not subject to chemical change before they reach the bone marrow or other sites of malignant growth.

With regard to the metabolism of the patient as a whole, the general principle to be followed in leuchæmia, as in other forms of malignant growth, is stabilization of the neutral fat of the body. This principle calls for careful planning in a rational interference with the patient's metabolism, instead of crude attempts to inhibit malignant growth by undirected damage of various tissues. The aim, in the words of J. P. Greenstein, is "to insinuate by subtle chemical means an inhibition of the master reactions responsible for unlimited growth and thus to use a delicate rapier to master the cancer rather than the bludgeons so far available or suggested".

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ALIMENTARY OBSTRUCTION IN THE NEONATAL PERIOD.[1]

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IT is acknowledged that all over the world there has been a steady fall in the infantile mortality rate during the period in which this has been a matter of interest. This fall has been due to many factors, ranging from better hygiene to the introduction of penicillin. However, this steady improvement has not appeared, except in minor degree, in the figures of neonatal mortality, and if any

[1] Read at a meeting of the Section of Pædiatrics, Australasian Medical Congress (British Medical Association), Sydney, August 20 to 27, 1955.

reduction is to be effected in infantile mortality as a whole, it is likely that it will result from better handling of the neonatal group.

A number of babies are born who, owing to extreme prematurity or to some serious congenital defect or abnormality, will inevitably perish. However, others have recoverable lesions, and important amongst these are babies with intestinal obstruction. In the absence of other abnormalities they should be eminently capable of normal survival once the obstruction is overcome.

That so relatively few of these babies do survive, in spite of vaunted improvements in methods of diagnosis, treatment and after-care, represents a grave challenge to the obstetrician, be he specialist or general practitioner, and to the pædiatrician. How is this challenge to be met?

Let us consider first the nature of the problem.

A study of the operation book and of the autopsy records of the Royal Alexandra Hospital for Children over a seven-year period, from July 1, 1947, to June 30, 1954, allowed the tracing of 498 children who were proved to have suffered from obstruction of their alimentary canals in the first month of life, and of these 133 died. This apparently fairly satisfactory state of affairs rapidly becomes a most unsatisfactory one, if one takes out the babies with hypertrophic pyloric stenosis (of whom there were 328, and of whom two died); the figures then become 170 babies admitted to hospital, with 131 deaths. Of these, 35 were judged from the records to have had a severe defect, or prematurity of a degree likely to prevent their survival. The deaths of the remaining 96 leave us with no grounds for complacency.

The types of obstruction which occurred, in order from the mouth downwards, are set out in Table I.

From Table I, it can be seen that the chief sites of obstruction (excluding the pylorus) were as follows: (i) œsophagus—40 cases (largely due to tracheo-œsophageal fistula); (ii) duodenum—33 (intrinsic lesions and *volvulus neonatorum*); (iii) small bowel—32; (iv) anus—23; (v) Hirschsprung's disease—15.

It is interesting to realize that in 63 of these 170 cases the obstruction was in the œsophagus and anus, and was therefore susceptible of early and easy diagnosis; but a baby with imperforate anus was admitted to hospital on the tenth day, and one with a tracheo-œsophageal fistula on the sixth day. A further patient with a tracheo-œsophageal fistula was said to have been successfully tube fed for several days. It behoves us, therefore, to pull up our diagnostic socks and to practise complete clinical honesty.

No one would seriously deny the great importance of early diagnosis in this problem. A wasted and dehydrated wreck means a headache for the "homœostatist" and a failure for the surgeon; and yet the warning signs are there to see, and do not differ greatly from those of the adult state.

It is of help in this regard to keep constantly before one the three questions posed by Wangensteen in his work on intestinal obstructions: (i) Is there an intestinal obstruction present? (ii) What is the site of the obstruction? (iii) What is the obstructing agent?

The answers to the first and second questions will most often be derived from the following considerations:

1. If there is an excess of saliva (or "mucus") because of inability to swallow; if respiratory distress and coughing are present because of overflow of saliva into the larynx; if there is choking, but not vomiting, on attempts at swallowing, with cyanosis; then the obstruction is probably œsophageal.

2. If there is intermittent vomiting of large amounts of recognizable food at intervals, perhaps of some duration, then the obstruction is at the gastric level.

3. If there are colic and shock, with progressive copious vomiting of bile-stained material, unrelated to the ingestion of food, and followed by abdominal distension and constipation, then the obstruction is in the small bowel. The higher the level of the obstruction, the more urgent are the symptoms likely to be.

4. If there are constipation and abdominal distension, sometimes with colic, followed after a variable interval by vomiting, then the obstruction lies in the colon. The lower the level of the obstruction, the less urgent are the symptoms and the more generalized is the distension.

TABLE I.
Types of Obstruction.

Type or Site of Obstruction.	Number of Cases.	Comments.
Œsophagus:		
(*a*) Tracheo-œsophageal fistula	37	
(*b*) Pure atresia	1	
(*c*) Congenital stenosis	1	
(*d*) Traumatic stricture	1	
Diaphragmatic hernia	2	Most of these babies present with acute respiratory distress, and have no time to show intestinal obstruction. The significance of hiatus hernia in neonatal vomiting could not be assessed from the material.
Stomach: hypertrophic pyloric stenosis	328	
Duodenal obstruction:		
Intrinsic causes (atresia, 6; stenosis, 5; uncertain, 3)	14	
Extrinsic causes	2	
Volvulus neonatorum	17	
Obstruction from duodeno-jejunal obstruction from bands	? 1	This is a very doubtful entity.
Jejunal obstruction:		
Intrinsic causes (atresia, 6; stenosis, 3)	9	
Extrinsic causes	0	
Ileal obstruction:		
Intrinsic causes (atresia, 12; stenosis, 4)	16	
Extrinsic causes	3	
Mesenteric thrombosis	2	
Patent omphalo-mesenteric duct with prolapse	2	
Meconium ileus	10	
Meconium peritonitis	5	
Obstruction due to hernia (inguinal, 2; internal, 1)	3	The site of the internal hernia is not known.
Colonic obstruction:		
Intrinsic causes	2	
Extrinsic causes	1	
Hirschsprung's disease	15	
Imperforate anus	23	
Paralytic ileus	4	

The change from the gastric symptoms to those of small-bowel obstruction takes place at the duodenal papilla in the second part of the duodenum, and is associated with the introduction of the large volumes of secretions from the liver and pancreas. Similarly the difference between small-bowel and colonic symptoms is determined by the ileo-caecal valve, and the protection which it affords (at least for a time) to the small bowel.

In answer to the third question (what is the nature of the obstruction?), the following may be said: (*a*) In a newborn infant, excess of mucus (saliva) *plus* choking and coughing on attempts at feeding raises the suspicion of a tracheo-œsophageal fistula. (*b*) Periodic vomiting of large amounts of saliva and food, usually related to meals, is likely to be due to hypertrophic pyloric stenosis. (*c*) Copious vomiting of bile-stained material, unrelated to meals, is pathognomonic of small-bowel obstruction, and may be due to atresia, stenosis or *volvulus neonatorum*. (*d*) Early failure to pass meconium may be due to imperforate anus; but if the anus and rectum are normal, and if

distension follows shortly, Hirschsprung's disease should be kept in mind.

The suspicion raised can most often be resolved in the following ways: in (*a*), by the passage of a soft rubber catheter into the stomach; in (*b*), by palpation of the tumour and the observation of gastric peristaltic waves in the epigastrium; in (*c*), by a plain X-ray examination of the abdomen, to visualize dilated loops of small bowel and fluid levels; in (*d*), by rectal examination, by radiography, and in Hirschsprung's disease by the relief of symptoms (in some cases) produced by the high passage of a soft rectal catheter or by a bowel washout.

If doubt remains, help may be gained by the judicious use of barium by the radiographer, and the microscopic examination of meconium for squame cells (Farber's test—the usual squames being absent in cases of complete antenatal obstruction).

The foregoing represents a considerable over-simplification of the problem, and is stated in positive terms. The following points in the different groups of cases require further emphasis:

1. Most of us would be surprised that œsophageal obstructions form the largest individual group. This has become apparent only because of the rise in numbers in recent years—a product of greater "awareness" of the condition. Every person who has the care of babies in obstetrics should be conscious of the significance of "mucus" in excess, and of avoiding feeding until patency has been proved by passage of a soft rubber catheter into the stomach. Otherwise inhalation of food weights the scales further in favour of pulmonary collapse and infection. Nearly half these children showed coincidental congenital abnormalities, and about one-quarter were premature. Such factors militate against a high survival rate.

2. The clinical picture of congenital hypertrophic pyloric stenosis is so well known, and operative treatment and results are so satisfactory, that no further comments of mine are necessary.

3. It is said that there is an association between Mongolism and duodenal obstruction, and Mongolism was seen in four out of 14 of our cases. The symptoms may rarely be of the gastric variety when the obstruction lies above the duodenal papilla. More commonly there is urgent bilious vomiting when it lies below this point. Epigastric distension and visible gastric peristalsis may be evident, but support for the diagnosis usually comes from a radiograph showing the dilated stomach and duodenum. At operation many sub-hepatic adhesions may be present, and their presence is a warning of something wrong. The establishment of a duodeno-jejunostomy is usually the indicated treatment.

4. There were 17 cases of *volvulus neonatorum*, of which 16 were of the classical type, the mid-gut loop being involved and the duodenum obstructed secondarily. The presenting symptom was vomiting in 15 cases. Bile staining was mentioned as being present in 10 cases, and the symptoms dated from birth in seven cases and from the first day in another five. Apart from two cases in which it was a presenting symptom, abdominal distension was noted in only four cases, pre-operative melæna in three cases, and hæmatemesis in one case. The picture is therefore similar to that of duodenal obstruction, except that in some cases the onset may be delayed for as much as nine days. In others it is possible that the symptoms subside, perhaps to recur at a later date. (One such patient was found, not included in the series, who had some symptoms at three days, but was not admitted to hospital until the fifth month.) Radiography is of help in the making of a pre-operative diagnosis by providing evidence of (*a*) duodenal obstruction—usually incomplete, (*b*) intestinal obstruction in some cases, (*c*) failure of descent of the caecum (barium enema).

5. Obstruction at the duodeno-jejunal junction from kinking of bands appears a very doubtful entity. The records of several cases in which such a diagnosis had been made at operation produced no evidence that undoing the "kink" had benefited the patients' condition, except possibly in one instance. It seems to me that to use the old non-committal term of duodenal ileus would be a better way of describing the dilated duodenum found at an exploratory operation for which no undoubted cause can be seen.

6. The classical clinical picture of small-bowel obstruction appeared, with vomiting of bile-stained material as the presenting symptom, followed shortly by abdominal distension. It is of interest that the onset of symptoms, even in cases of high obstruction, may be delayed for as long as four days, and the only feasible explanation appears to be delay in the establishment of alimentary secretions. However, I can find no information on this point in physiology text-books. Curiously enough, the patients with jejunal obstruction were almost exclusively female, and those with ileal obstruction almost exclusively male, but the numbers are too small to be significant. The most important feature of the records was the finding at autopsy on many subjects, some of whom had survived for ten or fourteen days after operation, that the anastomosis was anatomically patent, but that nothing had passed through it. From my own experience it is usual for the new stoma to open only on the fifth or sixth day, after the disappearance of œdema. Several theories may be postulated to show continued lack of relief of the obstruction after this period; the most important are (i) paralysis from distension, (ii) lack of potassium, (iii) neuro-muscular imbalance. I believe that the first of these is the correct explanation, and that results will be improved by the following measures: (*a*) emptying the grossly distended loops above the obstruction by direct suction at the time of operation; (*b*) forming a tube enterostomy just above the anastomosis to maintain this decompression, as the use of per-oral intestinal tubes does not seem satisfactory in very small babies. In the few cases in which this principle has been applied there has been a gratifyingly high proportion of recoveries.

7. Meconium ileus, secondary to congenital pancreatic fibrosis, is a relatively common form of obstruction of the small bowel. Abdominal distension is the early and striking clinical feature. In the present series vomiting, while usually present, was rarely prominent early, and only three out of the 10 patients are noted to have vomited bile. The palpation of doughy, sausage-shaped loops of bowel makes the diagnosis tolerably certain. The subsequent early respiratory death of these children, if they do survive, suggests that too active measures to secure their recovery (once the diagnosis is certain) may be regarded as misdirected enthusiasm, in view of the extra burden of distress put upon the parents by the mere postponement of the inevitable end.

8. Five cases of meconium peritonitis were found, in three of which the condition had obviously been present before birth. In three cases a perforation was seen, but in none was any cause for this uncovered. The condition was uniformly fatal. The outstanding clinical feature was gross abdominal distension, present at birth in three cases. Signs of fluid or gas, or both, were present, with vomiting as the chief symptom. Radiography usually gives a clear indication of the diagnosis; pneumoperitoneum, dilatation of the bowel with fluid levels, and calcification are the outstanding features.

9. Hernia was a rare cause of obstruction, while four cases of paralytic ileus occurred, in which dilatation of the whole alimentary canal, without obvious obstruction, was found. In one case this was apparently secondary to primary streptococcal septicæmia, and responded to the exhibition of antibiotics. The other three proved fatal.

10. Colonic obstruction, apart from Hirschsprung's disease and imperforate anus, is excessively rare; only two cases of atresia were found, with one instance of obstruction from external pressure through kinking over the edge of the pelvic mesocolon. The relatively high incidence of Hirschsprung's disease in this age group is of great importance. Few associated abnormalities were found, but there was a gross male preponderance of 13:1 (in one case the sex was not discoverable from the records). The symptomatology consists of vomiting, abdominal distension, and

constipation. Vomiting was absent in only one case, and this is somewhat at variance with the classical picture of colonic obstruction; but the vomitus was bile-stained in only two cases, and was not of the small-bowel obstructive type in the others. Abdominal distension became evident early, and both symptoms were present within the first forty-eight hours in almost every case. Constipation was apparently not a feature in three instances, and of these, one patient of my own had severe watery diarrhœa. However, constipation was noted in all the others from a very early stage, although to what degree it is difficult to determine. It is of interest that two patients died unexplained deaths with dramatic suddenness after manipulation of a colostomy; such a manipulation can be a dangerous procedure in a child.

11. Unlike the Hirschsprung's group, in the 23 cases of imperforate anus there was a very high proportion of associated abnormalities, 16 children being affected to some degree. This may form a partial explanation of the high mortality rate; but delays in diagnosis of from two to ten days occurred in six cases, in spite of the presence of symptoms. This should not be possible if a complete physical examination is made of every infant at an early stage.

Conclusion.

I have discussed only indirectly the differential diagnosis of neonatal obstruction, which is largely that of vomiting of the newborn. It must suffice at present to point out that the following signs and symptoms are danger signals: (i) excess of saliva in the mouth; (ii) the vomiting of bile; (iii) abdominal distension; (iv) constipation.

As the operation forms only an incident in the treatment of these patients, and as the after-care (particularly the administration of fluid and electrolytes) is a matter of supreme difficulty, it seems to me that the only real chance of improvement lies in the institutions used to handling such tiny patients. Early diagnosis and rapid transport to such a centre (with due regard to the risks of air travel to the gas-filled bowel of an infant with obstruction) would lead to improvement in the results.

I have endeavoured to point a pathway to early diagnosis. Even if doubt exists, no delay is allowable. If clinically evident dehydration is present, 100 to 150 cubic centimetres of fluid should be given by the subcutaneous route. Gastric suction should be instituted, and the child sent on at the earliest moment.

Reports of Cases.

CONTACT DERMATITIS FROM 18-CARAT GOLD.

By ERNEST CHENOWETH,
Melbourne.

THIS case is reported because of the rarity of commercial gold as an allergen, only one other case (Forster and Dickey, 1949) having been reported as far as I am aware.

Mrs. B., aged forty-five years, was referred with a history of having suffered from dermatitis of her hands and forearms for five years. The irritable rash first made its appearance on her left ring finger and later spread to her wrist and forearm. She had experienced similar trouble on the right hand and forearm, but in much milder degree. The original area at the site of the gold rings on her left ring finger was always the most heavily involved.

The history disclosed that when the left hand and forearm became too swollen, the rings were transferred to the right fourth finger, and returned to the left hand when the swelling subsided. They were worn much more on the left than on the right hand. Examination of the patient revealed acute dermatitis with vesiculation and spreading erythema centred around the rings on the left hand. There was also a patch of dermatitis beneath her gold watch.

Removal of the rings and watch and the application of hydrocortisone ointment healed the rash in a few days. Replacement of the rings caused a flare-up within a few hours, only completely relieved by their subsequent removal.

Reference.

FORSTER, H. W., JUNIOR, and DICKEY, R. F. (1949), "Case of Sensitivity to Gold-ball Orbital Implant: Eczematous Contact-type Dermatitis due to 14-Carat Gold", *Am. J. Ophth.*, 32: 659.

MANIC-DEPRESSIVE PSYCHOSIS FOLLOWING HEAD INJURY.[1]

By NEVILLE PARKER,
Psychiatric Clinic, Brisbane.

MANY causative factors have been considered in the ætiology of manic-depressive psychosis. These include hereditary and constitutional predisposition, biochemical changes, endocrine abnormalities, disorders of the diencephalon and emotional stress. Opinion is divided over the relative importance of organic and psychological factors in the production of this affective disturbance, and in the following case it is difficult to decide which predominates. However, the fact remains that an accident can transform a well-adjusted worker, with no apparent predisposition to manic-depressive psychosis, into a chronic mental invalid.

Clinical Record.

B. was born in 1905, the fifth child in a family of eleven. One sister was a congenital mental defective, and a brother was later discharged from the army with "nerve trouble". However, there was no other family history of nervous or mental disorder or of any hereditary illness. On leaving school at the age of fourteen years the patient joined his father as a blacksmith, and five years later worked as a mechanic in a brother's garage. He was a good tradesman and became a member of the Motor Mechanics Institute of Queensland. During the war years he was employed as a deputy foreman in the workshop of a large motor transport firm, and in 1946 he returned to his brother's garage. He had many friends and interests and appeared normal in every way; there was no suggestion of mood swings or periods of depression. He had married in 1934, and a son was born in 1939; outwardly the couple appeared to be contented and well adjusted, but the patient recalls that during the war years his wife was interested in a soldier who stayed with them when passing through Brisbane.

All went well until June 11, 1946. On this day he drove the family to the King's Birthday procession, and on the way collided with an army motor truck. He remembers leaving home, but the next thing he recalls is being nursed in the Brisbane General Hospital eleven days later. He had been admitted comatose and dangerously ill, and the following day his condition had improved to a restless stupor, in which state he remained for three days. Seven days after his admission to hospital he was able to complain of pain in his right shoulder, and a subluxation of the acromio-clavicular joint was diagnosed. There was no other evidence of localized injury, and an X-ray examination of the skull did not show any signs of fracture. The cerebro-spinal fluid was clear, no cells were present and the pressure was normal. He was discharged from hospital on June 25 (two weeks after admission) to be cared for by his wife, who had escaped all serious injury. While at home he was still confused and restless, had obvious loss of memory, talked a lot of nonsense, and imagined there were "crooks" everywhere in the house. He would be heard conversing with imaginary detectives, and at times he wandered away from home. He could not be managed, and was readmitted to the Brisbane General Hospital on July 27.

On his admission the confused restless state of mind was noted. There were no localizing signs in the central

[1] This case was presented at a meeting of the Queensland Branch of the Australasian Association of Psychiatrists, Brisbane, November 3, 1956.

nervous system, and examination of the cerebro-spinal fluid gave the following results: the pressure was normal; the protein content was 50 milligrammes and the chloride content 700 milligrammes, both per 100 millilitres; no cells were present, and the Wassermann and colloidal gold tests produced negative results. A second X-ray examination of the skull revealed no fracture. Three days later the right pupil was larger than the left, and a ventriculographic examination revealed dilatation of the left lateral ventricle but no displacement. This examination was repeated six months later and the appearance was substantially unchanged.

On August 12 confabulation was noted, and on August 18 affective disturbance was apparent—he talked continuously, wept readily, and at other times was infectiously cheerful and bright.

He was certified insane and admitted to the Brisbane Mental Hospital on August 30. At this time the pupils were equal, and no central nervous system abnormalities were present. Although he was complaining of impaired memory and concentration, there was no evidence of this on clinical examination apart from the amnesia following the accident. He was well orientated, and the only positive sign of illness was his hypomanic behaviour—everything engaged his attention and he talked rapidly with flight of ideas. He was discharged from the hospital in May, 1947, but there is no record of his condition at that time; no treatment had been given.

He stayed on a brother's farm, but did no work, and was readmitted to the Brisbane Mental Hospital in February, 1949, hypomanic behaviour being the outstanding feature. Again it was noted that he was well orientated, his memory was unaffected and he could give a good account of himself.

It is difficult to piece together his progress until November, 1949, when it was noted that he was depressed and complained of double vision. Ophthalmoscopic examination showed that this symptom was due to a congenital squint, and there were no abnormalities of the third, fourth or sixth cranial nerve. In 1951 he became hypomanic, and this condition was treated with sedation. In September electro-convulsive therapy was administered, and in all 20 treatments were given over a period of four months, when it was reported that he was a good worker, although at intervals he became very talkative.

Nothing significant is noted about his mental state until August, 1953, when he became depressed after a month's leave from hospital. After seven electro-convulsive treatments he was much improved and working in the ward again. He left hospital in March, 1954, and worked on a brother's farm for five months, and then came to stay with his aged parents. Depression gradually developed, but the relatives would not seek active treatment.

In July, 1956, he was convalescing in a private hospital from a varicocele operation when he was reminded of his wife by a clergyman, who, passing by, casually commented that he knew her—"a good woman". Shortly after his admission to the Brisbane Mental Hospital in 1946 she would have nothing to do with her husband, and after spending as much of their joint account as the bank manager would allow, she left to take up a new life in Sydney with her son. She never answered his letters and would not let the boy communicate with him. On the other hand, the patient continued in his affection for his wife, and when talking of her was readily moved to tears. He could not understand her attitude and longed to be reunited with her and to see his son. The clergyman's casual comment stirred him to visit her, and he was intercepted at the airport, noisy and elated, and returned to the mental hospital. He has now settled down and is a good ward worker.

At no time was he interested in claiming compensation, or was he particular about the way in which the £6000 damages he received were invested on his behalf; legal proceedings had been initiated by a brother.

Professor W. V. Macfarlane reported as follows on an electroencephalogram taken on March 26, 1956:

> This record is within the normal range of variation. There is a slight generalized divergence from regularity, but this would fall within normal limits. There is nothing to indicate a focus of injury. There are none of the slow wave patterns one would expect from a hypothalamic damage during trauma.

The following report was received from Mr. B. Fenelon, senior psychologist at the Psychiatric Clinic, who examined the patient in February, 1956:

> Tests were administered to measure his present level of intellectual efficiency and to assess if he had deteriorated intellectually.
>
> He achieved an I.Q.98 on the Bellevue Scale, Form 1. Probably at his best he would have shown good average general ability.
>
> Other tests administered included the Porteus Maze Test (T.Q. 93, Qualitative Score 15), Raven's Progressive Matrices (P.R. below 77 on Labour and National Service Dept. norms), Goldstein-Scheerer Colour-Form Test, two of the Babcock Learning Tests, and a Rorschach.
>
> The impression was that there existed a mild degree of organic impairment, but that factors arising out of an affective disorder were contributing strongly to his inefficiency. His state of depression appeared to be in partial remission.

Discussion.

Opinion is divided on the role played by head injury in precipitating psychosis, and the following three possibilities have to be considered: (i) The injury produces organic brain damage, which is directly responsible for the psychosis. (ii) Organic brain damage acts as a precipitating cause, exaggerating the preexisting personality traits of the patient. (iii) The accident produces disturbances in the dynamics of mental life, and the somatic trauma is not a direct ætiological factor (Gordon, 1934).

To many it would appear so obvious that a head injury produces organic brain damage to account for psychotic symptoms, that emotional factors would not be considered, and on reference to the literature one is struck by their absence in the reported histories. Those who believe in an invariable direct organic causation must postulate a temporary lesion, as many of these patients recover from their psychosis.

Schilder (1934) stated that he had never seen a case of manic-depressive psychosis in which the head injury was the only ætiological factor. Symonds (1937) believed that although the production of schizophrenic and paranoid states might involve other factors, the development of manic-depressive psychosis "strongly suggests that it is a direct result of organic disturbance". He described two cases in which the symptoms of manic-depressive psychosis developed before the patients had recovered from the acute traumatic psychosis, and considered that as a patient in his confusion could not be expected to appreciate the effects of his injury, this was a convincing argument in favour of his view.

From this one would infer that a person in a confused state following head injury could not sense emotionally important happenings. However, I do not agree with this. A patient confused and disorientated from senile brain changes can still be perceptive to emotional factors in his environment, and distinguish the relatives who have been kind from those uninterested in his well-being. The acute alcoholic, drunk to a state of confusion, is still able to sense the emotional tone of his environment, and the patient recovering from a general anæsthetic or insulin coma will settle down with a quiet nurse, whereas he may be restless and vociferous with a more aggressive attendant. It may be debated whether comparison can be made between these states of organic confusion and the confusion which follows a head injury, but the latter does suggest the possibility that gross emotional perception may be present although intelligence, orientation and memory are impaired.

Our patient can recall incidents which happened during this phase, and from his recollections it appears obvious that he was aware that his father-in-law was trying to cheat him. The belief that "crooks" were everywhere in the house may have been provoked by his father-in-law's

attempt, at that time, to induce the patient to sign over all his possessions to his wife. It is conceivable also that he may have sensed that all was not well with his wife.

Apart from the dilatation of the left lateral ventricle (and there is no knowing that it was not present before the accident), there is no supportive evidence of organic damage in this patient. The electroencephalogram and tests of deterioration do not suggest organic involvement; the validation of these tests, however, is open to question.

There is not sufficient evidence to invoke a direct organic causation, or to state that it acted to precipitate a latent psychosis. On the other hand, it is possible that the patient's wife used the accident as an excuse to escape from an unsatisfactory marriage, and that this loss of his wife was the important factor; it is well known how accidents are seized upon by people to rationalize their behaviour.

It is not contended that this case proves that the psychosis has had an entirely emotional causation, but it does throw doubt on Symonds's view that manic-depressive psychosis is directly due to organic brain damage. Like Rowbotham (1949), I believe that this can be neither proved nor disproved.

That "delusions' in the confused period have to be carefully assessed is shown in a similar case which Dr. B. F. R. Stafford has permitted me to record:

TABLE I.

Frequency of Psychosis following Trauma.

Source of Cases.	Number of Cases and Comment.
Queensland mental hospitals ..	2 cases in 4382 admissions (1951 to 1955).
United States mental hospitals (May).	0·3% of 70,987 admissions.
German Army in Franco-Prussian War (A. Meyer).	13 cases in 8985 cases of head injury.
Maudsley Hospital (Tennant) ..	44 cases in 13 years (1923–1936) (severe residual symptoms in 36%). Of seven of the 44 patients, five were depressive (three with depressive illness prior to the accident) and two were manic; four recovered, two entered mental hospitals, and one died.

T. was a normal out-going personality without any evidence of schizoid or paranoid tendencies. In April, 1944, he was involved in a car accident causing fracture of the jaw and base of the skull, concussion and minor abrasions. He stayed in hospital for three weeks and remained in bed at home for three months afterwards. In August that year, according to his wife, he began to show symptoms of being mentally sick—threatening her and committing acts of violence towards her.

He was admitted to the Brisbane Mental Hospital by Reception Order, the medical certificates purporting that the patient was suffering from paranoid delusions. They state: "He says there is a plot to rob him of his home and money. The conspirators in the plot are his wife, two friends, various doctors and a set of lawyers."

On admission to the Brisbane Mental Hospital he was well orientated and able to give a good account of himself. Apart from a few hours retrograde amnesia and two days amnesia following the accident, his memory was good for recent and remote events. Intelligence and affect were normal and physical examination revealed no clinical abnormality.

He stated that he had been estranged from his wife for six years prior to the accident, but they had lived together for the sake of their three children. They were continually quarrelling, and after he returned home from hospital his wife used every device to get hold of the £3000 compensation he was awarded. He claimed that she goaded him into assault and that his statements were an expression of domestic troubles rather than manifestations of insanity. He remained under observation for two and a half months and during this time there was no evidence of mental sickness. Statements from relatives confirmed his accounts of domestic disharmony.

He has remained perfectly well since his discharge from hospital.

That psychosis following trauma is a rare event can be seen from Table I.

Summary.

1. A case of manic-depressive psychosis following head injury is reported.

2. The possible mechanisms of its production are discussed with reference to the relevant literature.

3. Doubt is thrown on the common assumption that manic-depressive psychosis following head injury is invariably and directly due to organic brain damage.

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Reviews.

Pathological Histology. By Robertson F. Ogilvie, M.D., D.Sc., F.R.C.P.Ed., F.R.S.E., with a foreword by A. Murray Drennan, M.D., F.R.C.P.Ed., F.R.S.E.; Fifth Edition; 1957. Edinburgh and London: E. and S. Livingstone, Limited. 8¼" × 5½", pp. 494, with 334 photomicrographs in colour. Price: 52s. 6d.

FOR both medical undergraduates and graduates, Ogilvie's "Pathological Histology" is a very good book. That it has filled a need is borne out by the fact that since its first appearance in 1940 there have been five editions, and it has been reprinted twice. The book is based on a series of lectures on pathological histology, and has been designed as a companion to a standard text-book of pathology. The text includes brief descriptions of the macroscopic appearances of affected organs and tissues. The special feature of the book is that all the illustrations are reproduced from actual colour photographs of the stained sections. The illustrations, which now total 334, have been well chosen, and from the technical point of view are excellent. The text has been condensed to 468 pages.

No book on pathological histology can replace the study of histological preparations with the microscope; but this book has proved, and will continue to prove, a valuable aid to such study. The book reflects credit on author and publisher alike.

Outline of Fractures: Including Joint Injuries. By John Crawford Adams, M.D. (London), F.R.C.S. (England); 1957. Edinburgh and London: E. and S. Livingstone, Limited. 8¼" × 5½", pp. 256, with 218 illustrations. Price: 27s. 6d.

THIS is a well-produced small book, and the illustrations, over 200 in number, are of the high quality which we have come to expect from this firm of publishers. The photographs and line drawings are well chosen to reinforce the text, and the X-ray reproductions are adequate in quality.

The general principles of fractures and their treatment are dealt with in concise manner, but with full emphasis on the salient points of basic importance.

In a space of 176 pages, regional injuries receive consideration which is detailed without being over-burdened.

The approach is well-balanced and conservative for this metallic age, and the experienced author is evidently determined not to be guilty of leading the young astray.

With many possible roads to follow, there will always be argument as to the best route; here, however most of the methods of treatment outlined are well accepted, and it is only occasionally, as in the treatment of ankle fractures, that the personal preference of the author is allowed to intrude. Some will not agree with his indication for operation, and at the same time will hesitate to put back the clock twenty years in treating *os calcis* fractures conservatively on the "wait and see" principle.

It is of interest to see doubt cast on the efficiency of the traditional treatment of complete disruption of the acromioclavicular joint, and on the value of a walking caliper in fractures of the femoral shaft.

With its lucid and dogmatic style and good summaries, this book can be thoroughly recommended to the medical student; but general practitioners treating fractures will probably prefer larger and more detailed works.

A Synopsis of Regional Anatomy. By T. B. Johnston, C.B.E., M.D.; Eighth Edition; 1957. London: J. and A. Churchill, Limited. 8" × 5¼", pp. 460, with 20 plates and 19 text figures. Price: 28s.

PROFESSOR T. B. JOHNSTON'S "Synopsis of Regional Anatomy" now appears in its eight edition, six years after its seventh. As we have previously pointed out, its success lies largely in the fact that it covers adequately and clearly the essentials for the student within such a small compass that it holds out hope of his acquiring a coherent grasp of the subject—hope which he may have lost in contemplating the larger text-books. It is recommended that the book be not read before the completion of dissection. The *Nomina Anatomica* of Paris (1955) has not been introduced in the book as yet; but the term "lymphatic node" has been borrowed from it, to replace the misleading term "lymphatic gland".

Group Psychotherapy: The Psycho-Analytic Approach. By S. H. Foulkes and E. J. Anthony; 1957. London: Penguin Books, Wyman and Sons, Limited. 7" × 4¼", pp. 277. Price: 5s. 6d.

IN "Group Psychotherapy", S. H. Foulkes and E. J. Anthony describe the application of psycho-analytic theory and technique to group psychotherapy, which they are carrying out at the Maudsley-Bethlem Institute of Psychiatry. Following more recent developments in psychoanalytic practice, they deal with current relationships rather than with history and causation, matters which have already been studied before patients are referred to their department. In every therapeutic group difficulties arise over the assimilation of new members, who are liable to exhibit attitudes of avoidance or aggressiveness. The presiding psychiatrist or conductor sits in a circle of a group of some eight or ten patients, the circle bearing a symbolism, such as "magic circle" or "circle of friends", and providing the opportunity of watching a patient bringing his chair in closer or pushing it further out. As therapy progresses, "I" is gradually changed to "we", and the group becomes a true community. Usually forty or more sessions of at least one hour are needed, at the rate of one or more a week. The authors describe the modifications which they have introduced for groups of children, and discuss the possible applications of their methods to other groups which may not have a primary therapeutic aim. This book will interest not only psychiatrists and those who are conducting classes for the remedying of physical disabilities, but also ministers of religion and sociologists.

Materia Medica and Pharmacology: For Nurses. By J. S. Peel, M.P.S.; 1957. Christchurch, New Zealand: N. M. Peryer, Limited. 8½" × 5½", pp. 184, with illustrations. Price: 24s.

THIS book, first published in 1955, is now in its second edition. It is written by Mr. J. S. Peel, who is a well-known hospital pharmacist in New Zealand. Mr. Peel had briefly, but successfully, surveyed the *materia medica* in the first edition of his book; but the introduction of new drugs and therapeutic measures is so rapid today that such a book is almost out of date as soon as it is widely available.

This book is intended as a text-book for nurses in training, and the early chapters deal with weights and measures, prescription writing, and a certain amount of forensic material relating to the control of dangerous drugs. The author then goes on to classify drugs in a pharmacological scheme, and here one must point out that several errors are apparent. The term "sympathetic" is used to describe the autonomic nervous system; this is not normally accepted and must cause confusion. Some unusual terms are also introduced. Ergometrine is described as having an "anti-orthosympathetic effect"; this, apart from the use of this very unsatisfactory term to describe an adrenolytic effect, surely involves a misprint for ergotoxine or ergotamine. One wonders again why atropine is cited as an antagonist to digitalis, especially after the author has given as his definition that antagonists exert pharmacologically opposite actions; one would immediately think of anæsthetics and analeptics in looking for such an example.

The grouping of the antihistamines as powerful or less powerful is unfortunately incorrect, since mepyramine is more powerful than promethazine, but the durations of action of the two are entirely different, and it is on this basis that they are selected in therapeutics.

In a short note on pH, the author attempts to simplify this subject for his readers, and in doing so creates the impression that pH accurately defines the acidity of a solution without reference to the degree of buffering which may be present—a most important consideration in preparing solutions for injection. Unfortunately, such errors are numerous, and will create difficulties for students who may later wish to obtain further information from more advanced text-books.

The book is useful in its general scope and simple presentation; but it is a pity that standard terminology has not been used in the physiological considerations of the subject, and that so much has been sacrificed for simplicity.

Positioning in Radiography. By K. C. Clark, M.B.E., F.S.R.; Seventh Edition; 1956. London: Ilford, Limited, William Heinemann (Medical Books), Limited. 11¼" × 9", pp. 656, with 2150 illustrations. Price: 105s.

THE first edition of this book was published in 1939, and it has proved so popular that six more editions have been required. The book is much enlarged, and most of the work has been carried out in the technical section of Ilford, Limited. The various positions for the taking of films are shown by very good photographs, the various technical factors are given and the resultant radiograph is displayed. The methods of examining the skull are clearly depicted by photographs and diagrams, and beautiful films are shown of such difficult regions as the optic foramina, the mastoid areas, the petrous temporals *et cetera*. An ingenious method of showing the tarsal sesamoids by tangential views with the great toe extended is described. The vertebral column is studied in great detail in every section of its course. Many new positions for radiographing the shoulder are described and should prove most valuable. All the up-to-date methods employed in examinations of the gall-bladder and renal areas, both normally and with the use of contrast media, are dealt with in detail. Considerable space is devoted to dental radiography, and good descriptions are given of miniature radiography and cineradiography. There are supplements on contrast media, exposure tables, risks to the patient and metric equivalents. The book is the most outstanding work published in this field, and a copy should be available in every department of radiology.

Sex in Christianity and Psychoanalysis. By William Graham Cole; 1956. London: George Allen and Unwin, Limited. 8½" × 5½", pp. 343. Price: 21s.

To review this book adequately one would need to be a philosopher and a theologian, as well as a psychiatrist. As its title indicates, the book summarizes the attitude to sex of the great Christian leaders from Jesus and Paul to Fulton Sheen and Reinhold Niebuhr, in addition to the interpretations of sex offered by psychoanalysts. Nevertheless, the book will be of great interest and usefulness to psychiatrists, psychologists and social workers, because it will help them to understand the influence of the Church on the sexual *mores* of their patients. The author stresses the Bible's positive, naturalistic approach to sex and the body. This is in contrast with the negative, dualistic attitude of the early church, which he traces to earlier Greek influence. The author is Chaplain, Associate Professor and Chairman of the Department of Religion at Williams College, Massachusetts, United States of America, and writes from the Protestant point of view.

The chapters dealing with psychoanalytical interpretations of sex give useful reviews of the work of Freud, Karen Horney, Franz Alexander and Sandor Rado, all of whom have made original contributions in this field. Unfortunately, there is little reference to the work of British or Continental psychoanalysts, or to that of Havelock Ellis, Hirschfeld and others. Alfred Kinsey comes in for some pungent criticism.

The final chapter is the author's own attempt to present a synthesis of the Christian and psychoanalytical perspectives. In view of the differences of opinion on sex in both Christian and psychoanalytical circles themselves, let alone the fundamental divergences between the two approaches,

the task would seem to require courage and ingenuity beyond the reach of anyone at the present stage of evolution of our knowledge. What the author does, in effect, is to present his own interpretation of the Biblical revelation concerning sex, and to show how this Divine revelation, given some two thousand years ago, anticipated some of the "discoveries" of modern psychoanalysts, such as the importance of inner motivation compared with the legalistic impositions of church and society. This he does with a tolerance which is bound to cause some emotional reactions and (we hope) some hard thinking in both theological and medical circles. For instance, he states in one place that "theological orthodoxy is decidedly secondary in significance to existential wholeness", and in another place that "the two terms (sin and neurosis) have been used more or less synonymously in the preceding pages, regarding them both as rooted in anxiety".

The book is well bound and printed, and has a useful index. The literary style improves as the book proceeds, being rather repetitive, loose, and occasionally irritatingly jocular in the early portions. On the whole, however, it provides an interesting, helpful and provocative pilot study in a field which needs much further cultivation.

Principles of Epidemiology. By Ian Taylor, M.D., M.R.C.P., D.P.H., and John Knowelden, M.D., D.P.H.; 1957. London: J. and A. Churchill, Limited. 8½" × 5½", pp. 308, with 26 illustrations. Price: 30s.

DR. IAN TAYLOR, an epidemiologist of the London County Council, and Dr. John Knowelden, of the London School of Hygiene, have written this book to fill a noticeable gap in this field. A student of human epidemiology will naturally consult the well-known texts of Topley and Wilson, of Greenwood or of Stallybrass. The first is orientated too much towards the bench, even though Topley was especially interested in herd immunity, and is too brusque in its treatment of the necessary statistics. Greenwood's books have too personal a touch for general appeal, while the work of Stallybrass and some other epidemiological texts are too loaded with rather cumbersome mathematical computations and speculations. Taylor and Knowelden have succeeded in giving an account of human (perhaps one should say English) epidemiology, suitable for public health workers and epidemiologists. The necessary statistical rates are defined and used to make observations of human communities effective. The usual infective diseases of children are well handled. The references are well chosen from English and American sources, although one is surprised to find no mention of Creighton. The Thomas Farr of the text and index is, of course, William Farr. Table 14 gives reservoirs of infections, but has no mention of malaria; nor do malaria, plague or helminthic diseases appear in the index, although plague is discussed in the text. The authors agree with the modern view that epidemiology should be used in a wide sense, which is a reaction against a view that only infective diseases should be included. Of course, this narrow definition would make it impossible to know initially whether a problem should be studied by an epidemiologist. We may think of ergot poisoning or cancer as examples. The book can be warmly recommended.

Studies on the Distribution of Tritium-Labelled Dihydrostreptomycin and Tetracycline in the Body. By Torsten André; 1956. Stockholm: Acta Radiologica (Supplement 142). 9½" × 7", pp. 92, with 41 illustrations. Price: Sw. Kr. 25.

THIS book is published as a supplement to the journal *Acta radiologica*, and is an account of an investigation undertaken by the author. It is, in fact, a research monograph.

The subject matter is divided into ten chapters, four of which deal with the techniques of preparing radioactive dihydrostreptomycin and tetracycline, the use of the autoradiographic technique, and the counting methods which the author has employed. The remaining chapters describe the results obtained, and deal with the gross distribution of these antibiotics in the animal body, the passage through capillary walls, the penetration into abscesses, the local application of these drugs and their stability in the body.

The book is very well produced and illustrated, with many fine autoradiographic pictures, and the translation is faultless. This is essentially a book for the research worker in chemotherapy; but it is also a valuable guide to the techniques for the study of drug distribution and metabolism, and should interest many others who wish to avail themselves of such modern methods in their research. The author appends a good bibliography, dealing primarily with the absorption, fate and distribution of streptomycin and the tetracyclines.

This is a research thesis, and will find appropriate recognition as such.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Paths to Peace: A Study of War, Its Causes and Prevention", edited by Victor H. Wallace, M.D. (Melb.), F.R.C.S. (Edin.); 1957. Melbourne: Melbourne University Press. London and New York: Cambridge University Press. 8½" × 5½", pp. 418. Price: 25s.

The points of view of many leaders of thought in Australia brought together in an integrated whole, with a foreword by Jawaharlal Nehru.

"Surgery of the Anus, Anal Canal and Rectum", by E. S. R. Hughes, M.D. (Melbourne), M.S. (Melbourne), F.R.C.S. (England), F.R.A.C.S.; 1957. Edinburgh and London: E. and S. Livingstone, Limited. 9½" × 6½", pp. 316, with 276 illustrations. Price: 50s.

The author's aim has been not to write a work of reference but to describe theory and practice in the surgery of the anus, anal canal and rectum which he has found to be adequate.

"Pioneer Surgeons of the Woman's Hospital: The Lives of Sims, Emmet, Peaslee, and Thomas", by James Pratt Marr, M.D.; 1957. Philadelphia: F. A. Davis Company. Sydney: Angus and Robertson, Limited. 9" × 6", pp. 160, with illustrations. Price: 60s. 6d.

The story of four surgeons who worked at the Woman's Hospital in the State of New York in the last half of the nineteenth century.

"Being Lived by My Life: A Sort of Autobiography", by Charles Berg; 1957. London: George Allen and Unwin, Limited. 8½" × 5½", pp. 256. Price: 21s.

A psychoanalyst tells his own story.

"Textbook of Medicine", by various authors, edited by Sir John Conybeare, K.B.E., M.C., D.M. (Oxon.), F.R.C.P., and W. N. Mann, M.D. (Lond.), F.R.C.P.; Twelfth Edition; 1957. Edinburgh and London: E. and S. Livingstone, Limited. 9" × 6½", pp. 877, with 39 illustrations. Price: 42s.

Revised and largely rewritten since the previous edition of 1954.

"Sodium-Restricted Diets and the Sodium Content of Foods", prepared by The Nutrition Section, Commonwealth Department of Health, Canberra; 1956. Canberra: The Australian Institute of Anatomy, Commonwealth Department of Health. 9½" × 5½", pp. 40, with tables. Price: Free for the medical and nursing professions.

Discusses restriction of sodium, sources of sodium and the preparation of sodium-restricted diets.

"A Manual of Human Anatomy: Volume 3: Abdomen", by J. T. Aitken, M.D., G. Causey, M.B., F.R.C.S., J. Joseph, M.D. M.R.C.O.G., J. Z. Young, M.A., F.R.S.; 1957. Edinburgh and London: E. and S. Livingstone, Limited. 8½" × 5½", pp. 144, with 29 illustrations. Price: 12s. 6d.

"A Manual of Human Anatomy: Volume 5: Central Nervous System", by J. T. Aitken, M.D., D. A. Sholl, B.Sc., and J. Z. Young, M.A., F.R.S.; 1957. Edinburgh and London: E. and S. Livingstone, Limited. 8½" × 5½", pp. 148, with 40 illustrations. Price: 12s. 6d.

Two volumes of a five-volume practical work on anatomy for medical students.

"Sydney Looks Back", by Isadore Brodsky; 1957. Sydney, London, Melbourne, Wellington: Angus and Robertson. 8½" × 5½", pp. 256, with many illustrations. Price: 42s.

A series of sketches of Old Sydney.

The Medical Journal of Australia

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All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

THE TROUBLESOME STAPHYLOCOCCUS.

STAPHYLOCOCCAL INFECTIONS are amongst the most disquieting problems in medicine today. The difficulty experienced in their prevention and treatment is something of an anachronism in an age in which we like to think that the infectious group of diseases is conquered or in sight of being conquered. How far this difficulty is the direct result of antibiotic therapy, whether rightly used or abused, is a matter for argument—the question varies with how we approach it, and generalizations tend to be misleading. It is clear, on the other hand, that the wide use of antibiotics has brought the problem of the staphylococci into prominence; they have always been something of problem children among the pathogenic organisms, and they are gaining even more limelight as time goes on. At the annual meeting of the Australian Pædiatric Association in Canberra earlier this year, the discussion took on new life with the introduction of the subject of staphylococcal infections. It seemed that nearly everyone wanted to talk about it, not because they all knew the answers to the problem, but because it had obtruded itself in a forceful and perplexing way on pædiatric practice, as it has done elsewhere. Large and well-managed children's hospitals have found themselves baffled by outbreaks of staphylococcal infection of the lungs, with a depressing mortality rate.

This is, of course, not just an Australian phenomenon. At the Children's Hospital, Winnipeg, for example, there have been 12 deaths in 27 cases of staphylococcal pneumonia in infants and young children in a period of two and a half years.[1] J. N. Briggs, who reported these cases, states that the relationship of exposure in hospital is difficult to assess, but it would seem to fit in with the theories of an excessive exposure or an increase in pathogenicity of the organism already present, for in this series of 27 children, four had previously been admitted to hospital, three for trivial complaints such as colic and one for pyloric stenosis. Two of these children died from staphylococcal pneumonia, which they developed while in hospital. The general experience is, of course, that a great many staphylococcal infections appear to originate in hospitals, and this is one of the most disturbing features of the whole problem, especially as it seems often to be associated with the indiscriminate use of antibiotics. G. A. Gresham and M. H. Gleeson-White[2] have reported 14 fatal cases of staphylococcal bronchopneumonia in debilitated hospital patients, and all the cases were regarded as being the result of hospital cross-infections. One difficult feature of this particular series was that in only four of the 14 patients had a lung infection been diagnosed during life. This meant, of course, that there could be no possibility of treatment with the appropriate antibiotic, which, given early enough, offers the only hope of recovery in these cases. Gresham and Gleeson-White state that the pattern of resistance to penicillin, streptomycin and chlortetracycline shown by the strains of *Staphylococcus aureus* isolated from the lungs of these patients leaves little room for doubt that they were all "hospital" staphylococci. The rapidly increasing pollution of the hospital environment with antibiotic-resistant organisms of all kinds suggests that this type of staphylococcal pneumonia is likely to become one of the most serious cross-infection hazards that the debilitated patient has to face in hospital. Another side of the picture is seen in a report by J. Cook *et alii* of two outbreaks of staphylococcal diarrhœa involving 31 patients who had received antibiotic therapy at the Radcliffe Infirmary.[3] The chief cause of the diarrhœa was infection with *Staph. aureus*, which was grown from the fæces of 20 of the patients. Fourteen of the 31 patients died. Of the 31 patients, 14 had had partial gastrectomies, and seven of these were among the 14 who died. Of the total number of cases, 17 occurred in one male surgical ward, where the incidence of the disease reached the proportions of a small outbreak in the spring of 1954. In view of the fact that in the Radcliffe Infirmary staphylococcal diarrhœa has become the major cause of death after elective partial gastrectomy, and the equally unhappy experiences sometimes associated with the treatment of medical patients by means of antibiotics, Cook and his colleagues submit that the routine prophylactic use of antibiotics is not justified. They state that the relatively insoluble sulphonamides provide adequate preparation for colonic surgery, and it is unnecessary and even dangerous to use antibiotics in order to prepare the patient for operation, even on the stomach or on the unobstructed small bowel. However, if post-operative complications

[1] *Canadian M. A. J.*, February 15, 1957.
[2] *Lancet*, March 30, 1957.
[3] *Brit. M. J.*, March 9, 1957.

ensue, or if definite indications are present at operation—for example, a grossly soiled peritoneal cavity—the appropriate antibiotic should be used, at full strength and in short courses. In conjunction with these measures, every effort must be made to reduce the number of *Staph. aureus* organisms in the environment of the patient, not only to avoid surgical sepsis, but also to allow the safe and effective use of antibiotics when this is necessary. Practical measures designed to this end are discussed in some detail. It is of interest, in passing, to refer to a recent report by D. Gordon, J. Macrae and Dorothy M. Wheater[1] on the use of a Lactobacillus preparation in conjunction with antibiotics. They point out that the chief cause of diarrhœa associated with antibiotic therapy is thought to be the partial destruction of the natural intestinal flora. In the absence of competition and of inhibitory substances, such as lactic acid and hydrogen peroxide, produced by the normal flora, antibiotic-resistant pathogens can flourish, and the risks of this happening grow greater as resistant strains become more prevalent. On the theory that such side effects might be prevented if, during antibiotic therapy, saprophytic organisms were introduced into the bowel in sufficient numbers to become established, they studied the result of the administration of *Lactobacillus acidophilus* in conjunction with oral antibiotic therapy. Sixty-six patients receiving tetracycline by mouth were divided into two groups, one of which was given a preparation incorporating antibiotic-resistant strains of *L. acidophilus*. Fæcal specimens from all patients were examined bacteriologically at intervals before, during and after treatment. It was found that the staphylococci increased in both groups at the beginning of antibiotic therapy. Staphylococci continued to increase in number in the patients taking the antibiotic alone; but in those taking the lactobacilli, a pronounced drop in numbers followed the initial rise. Simultaneously in this group, the lactobacilli were rapidly established and continued to multiply. This followed the elimination of the normally non-resistant lactobacilli by the antibiotic during the early days of treatment.

The instances of staphylococcal infection that we have quoted are just random samples of what is a widespread major problem, but they serve to highlight how serious a problem it is. Its solution will probably involve the most thorough clinical and academic investigation of the essential nature of the problem, to be followed by thorough practical application of appropriate measures. A good start towards the understanding of the problem will be found in a review of the question by David E. Rogers.[2] He states that, despite the apparent close biological relationship between staphylococci and other Gram-positive cocci which produce acute human infections, there is increasing evidence to suggest that staphylococci may differ from these microorganisms in fundamental humoral-cellular relationships within the animal or human host. Certain biological properties of staphylococci may have a bearing on the pathogenicity and chronicity of staphylococcal infections. By the same token, recent experimental studies suggest that certain host mechanisms or changes in host resistance may serve to perpetuate staphylococcal infection, or to convert the staphylococcal carrier state into active disease. The clinical situations in which serious staphylococcal infections arise at the present day differ in many important aspects from the clinical syndromes noted during the pre-antimicrobial period. There is abundant evidence to indicate that antimicrobial therapy has not been successful in dealing with a number of the serious staphylococcal infections seen in hospital patients today. Rogers brings evidence to show that there are unique features in staphylococcus-host relationships which set the staphylococcus apart as a highly adaptable parasite, capable of surviving within human serum and phagocytic cells, and adjusting itself to meet unfavourable new environments, including human tissues bathed in antimicrobial substances. He states that the population group now developing staphylococcal infections is in certain important ways a different group from that acquiring staphylococcal infections during the period before antimicrobial agents were available. In general these patients are individuals with advanced, serious and potentially fatal disease, who acquire staphylococcal infections within the hospital. The increasing incidence of infection in this group due to strains of staphylococci which are not susceptible to many antimicrobial agents constitutes a disturbing problem. Nevertheless, it is difficult to attribute our therapeutic failures to drug-resistance alone in a significant number of cases. A basic underlying disease, upon which staphylococcal infection is superimposed, is commonly the important factor in determining the outcome. In this era of antimicrobial coverage, the staphylococcus appears to have displaced the pneumococcus as the invader in terminal illness. Rogers goes on to point out that the healthy human host possesses a high degree of resistance to infections due to staphylococci. There are recent indications that the circumstances which lead to altered host resistance can be approached and defined experimentally.

It appears probable that staphylococcal infections, once initiated, will continue to cause the death of a number of seriously ill patients who now constitute a large part of our hospital populations. In Rogers's view, it is doubtful that new antimicrobials will alter this situation, and indeed there is much to suggest that antimicrobial agents have played a role in the emergence of staphylococci as a troublesome hospital problem. More information is needed about the factors which increase host susceptibility to staphylococcal infection. Procedures which will effectively reduce staphylococcal carrier rates and cross-inoculation of staphylococci within hospitals also require better definition. As Rogers states, the therapy of established staphylococcal infection has received the major emphasis in recent years. Methods which may prevent staphylococcal infections in normal or abnormal hosts now merit equally serious investigation, in the hope of reducing the hospital incidence of staphylococcal disease with its relatively high mortality. Certain practical measures are, of course, already known, and would yield dividends if they were faithfully followed. One is the intelligent and restrained use of antibiotics, and in particular the conservation of such antibiotics as erythromycin for emergency use. Another is the careful implementation of measures that have long been established as of value in limiting cross-infection within hospitals.

[1] *Lancet*, May 4, 1957.
[2] *Ann. Int. Med.*, November, 1956.

Current Comment.

SPREAD OF THE NEW INFLUENZA VIRUS OUTSIDE ASIA.

THE new influenza virus responsible for the present widespread epidemics in Asia has now been imported into Europe and Australia and is believed to have been seeded in the North American continent, according to reports reaching the World Health Organization and recorded in a summary dated June 14, 1957. So far, however, although the virus is believed to be extensively seeded in these new areas, it has caused no outbreaks of the disease, and it is hoped that it will not do so during the summer season. Officially classified as Virus A/Singapore/1/57 (because it was first identified by laboratory tests in that city), the new virus has been isolated in Australia (in Victoria and at Cairns) and in the Netherlands (at The Hague). In the United States, patients with influenza were reported arriving by ship in San Francisco, California, but the presence of the virus has not yet been proved by laboratory tests.

All reports received by the World Health Organization continue to stress that the disease caused by this virus remains mild. Very few deaths have been scientifically proved to be due to this cause; most are among elderly people suffering from chronic bronchitis. There is still no cure for influenza, as the virus does not respond to antibiotics or other treatment, but penicillin and similar drugs remain the weapon of choice against the complications (*e.g.*, pneumonia) which may arise in the course of the disease. A useful summary of the characteristics of the outbreak and details of a typical attack, as observed in Malaya, will be found in the communication from Kuala Lumpur published in this journal on June 26, 1957, at page 929. The authors, two workers at the Institute of Medical Research and a general practitioner, make it clear that, despite a high incidence and variation in the clinical severity, the disease has been more of a nuisance than a threat to life or permanent health.

In order to prevent further outbreaks of this new type of influenza, vaccine production has begun in several countries starting from virus specimens collected and distributed by the World Health Organization to its 57 influenza centres in 46 countries. The work is coordinated by the World Health Organization's World Influenza Centre, in Mill Hill, London, under the direction of Dr. C. H. Andrewes, and by the International Influenza Center for the Americas, Montgomery, Alabama. The World Health Organization believes that it is impossible to stop the spread of influenza by quarantine, because such measures are as costly as they are ineffective. It is considered that there should be minimum interference with world traffic, but acutely ill patients should be isolated.

The epidemic situation, as described in reports received by the World Health Organization, is as follows. Influenza has now spread to most areas of Japan and Indonesia; it is now present in the Philippines, in Vietnam, Thailand and India and in two towns of Pakistan (Karachi and Lahore). It is starting in Burma and abating in Cambodia and Borneo. No cases have yet been reported from Korea, East Pakistan and Ceylon. In Burma an influenza outbreak is starting in Rangoon and Moulmein. The occurrence of sporadic cases or a mild incidence of influenza is reported in all provinces of Indonesia; at Djakarta the weekly number of deaths has been above average, and the epidemic is still spreading. Thailand reports in the Bangkok area 73,000 cases up to June 3, and 48,000 cases between June 4 and 8. Influenza has spread all over Japan; schools and classes were closed by June 1 in 18 prefectures, of which 15 were on the main island. In Pakistan, the presence of a few cases of influenza, of which one was among arrivals from Singapore and one from Bombay, was detected at Karachi by June 6; some 150 cases were reported at Karachi and less than 50 cases at Lahore by June 11. In the Philippines, about 185,000 cases with 441 deaths ascribed to influenza were reported during the week ended June 1. In Vietnam, about 2300 cases were recorded in the Saigon area; the presence of the infection was also reported in the provinces south and south-west of Saigon. In Australia, early in May, cases of influenza-like illness appeared among a group of Europeans who arrived by air from Europe via Singapore; a fairly sharp outbreak of mild influenza then appeared in the community in Victoria. Virus strains isolated in connexion with this outbreak and from a member of the crew of a ship from Singapore at Cairns, Queensland, were indistinguishable from the strain A/Singapore/1/57. Two cases of influenza were also recorded in Darwin, Northern Territory, in the middle of May. A report dated June 6 indicates that, apart from mild influenza disease at Darwin, there is no evidence of a spread of influenza in Victoria or at Cairns. By the end of May, there was no increase in absenteeism in the government offices in the capital cities of each State. In the United States of America, the presence of patients suffering from influenza was reported on board a ship which arrived at San Francisco, California, on June 9. The introduction of infection by the A/Singapore/1/57 strain of virus into the United States was considered on June 7 to be a distinct possibility, because persons who have been in Asia recently are entering the States in substantial numbers and are dispersing to all parts of the country. In the Netherlands, a case of clinical influenza at The Hague in a patient who arrived by air from Djakarta (Indonesia) on June 4 was identified by virus isolation as due to A/Singapore/1/57 strain, which was also considered responsible on serological grounds for cases among the passengers of a ship at Rotterdam on May 27.

THE INCIDENCE OF GLANDULAR FEVER.

GLANDULAR FEVER is a disease which is notifiable in only a few parts of the world. It is a fashionable disease, although by no means brand new. Its protean nature and in particular the fact that it commonly presents with sore throat and malaise are responsible for both misdiagnosis and suspicion. Quite often in practice one will encounter a patient in whom one suspects glandular fever; and while the diagnosis is probably correct, time and circumstance, coupled with the patient's improvement, are responsible for one's neglecting to prove the matter conclusively. It is certain that at least as often, and probably much more often, glandular fever, by virtue of its frequently mild manner, is not diagnosed at all.

In recent years pathologists in public and hospital departments in England and Wales have been making voluntary reports upon cases of infectious diseases diagnosed by them. One of these diseases is glandular fever. K. W. Newell[1] has analysed 1769 such reports. He is careful to point out that his information is only fragmentary; however, much of his material is of interest and value. His figures show that 61% of cases occurred in the age group fifteen years to twenty-four years. The overall sex distribution was even. Below the age of fifteen years and above the age of twenty years the incidence of glandular fever was equal in males and females, but in the age group fifteen years to nineteen years only 39% of cases occurred in males. There was no seasonal variation in children, but cases in adults showed a summer and autumn preponderance. There was no evidence of glandular fever in epidemics, although occasionally groups of cases occurred in a district over a short period. When the distribution of patients throughout the country and the occupations of patients were studied, the incidence of glandular fever was seen to rise in association with the availability of diagnostic centres. This observation is open to several interpretations, of which the most charitable is that the true incidence of glandular fever is much higher than has been hitherto suspected.

[1] *J. Clin. Path.*, February, 1957.

Abstracts from Medical Literature.

OPHTHALMOLOGY.

Certain Modifications in Minor Lachrymal Instruments.

J. FOSTER (*Brit. J. Ophth.*, November, 1956) suggests the following alterations in instruments used for syringing and probing the tear duct. The cannula should be narrowed to 0·55 millimetre (24 standard wire gauge) and shortened to five-eighths of an inch in length. It should be attached to a Luer-Lok syringe to prevent "blow-back". The punctum dilator should be made of stainless steel and have added to its opposite end a very fine pointed dilator for dilating minute puncta (a "finder"). Probes should have a grooved disk-shaped handle, and be modified to the form employed by Maddox in his hollow suture-passing probe. They should be marked on the obverse side with the diameter in millimetres—from 0·6 to 1·4 (0·6, 0·8 and 1·0 millimetre are the most useful).

Failure in Congenital Cataract Surgery.

F. C. CORDES (*Am. J. Ophth.*, January, 1957) lists the complications of surgery in congenital cataract. He places glaucoma, pupillary displacement or occlusion and retinal detachment at the top of the list; corneal changes, epithelialization of the anterior chamber, uveitis, sympathetic ophthalmia, endophthalmitis and panophthalmitis occur much less frequently. He analyses the results of a histo-pathological examination of 56 eyes removed after various operative procedures for congenital cataract, and finds that 46% of the patients had glaucoma and 41% had retinal detachment (the average interval for the appearance of detachment being 22·2 years after the last needling). He draws the following conclusions: (i) Linear extraction is the safest procedure. (ii) If the pupil will not dilate well, a full iridectomy is mandatory. (iii) Multiple needlings seem to be the least desirable of all procedures. (iv) Early restoration of the anterior chamber at the conclusion of the operation by the injection of air is a worthwhile procedure.

Air in the Eye.

A. LISTER (*Brit. J. Ophth.*, February, 1957) enumerates the uses of air in the eye. He stresses the fact that the patient should be kept reasonably flat with not more than three pillows for the first day or two after operation, to avoid the only likely serious complication, which is the passage of air over the pupil behind the iris, where it does the opposite of what is desired. He believes it to be contraindicated when there has been a complete iridectomy, and certainly when there has been a vitreous loss. It is useful in penetrating keratoplasty, in total keratoplasty, and in cyclodialysis. However, perhaps the greatest value of air is in the repair of a perforated eye, in which it is extremely difficult to ensure that uveal tissue, lens capsule or vitreous is clear of the wound. The final use of air is in the treatment of retinal detachment. It is found to be of advantage particularly in upper quadrant detachments, and the patient may be nursed in Fowler's position with the detachment being kept in place by a large bubble of air. Cases are recorded to illustrate how air is useful in overcoming gravity in the elderly patient, and in controlling a totally detached retina. The third possible action worth mentioning in a detachment is in breaking down adhesions between vitreous and retina which would prevent the replacement in the latter. As the effect of an air injection upon the vitreous itself is not known, there is no question of advocating it in more than the minority of cases of retinal detachment, and it is in fact contraindicated when there is a particularly large tear, owing to the risk of air passing behind the retina. The author believes that saline is to be preferred to air when it fulfils the desired purpose.

Prognosis in Strabismus and Orthoptic Treatment.

T. K. LYLE AND J. FOLEY (*Brit. J. Ophth.*, March, 1957) deplore the practice in many clinics of the routine course of orthoptic treatment, which is recommended and carried out indiscriminately in all cases of non-paralytic strabismus. They suggest that proper selection of cases will result in a higher proportion of patients with good binocular vision and save the needless worry and expense at present being undergone by large numbers. Results depend on the following factors: (*a*) the age of the patient; (*b*) the age at onset of strabismus; (*c*) the mode of onset (that is, constant from onset or intermittent); (*d*) the duration of the strabismus before the visual axes are aligned by operation or other means. The following conclusions are drawn in relation to non-paralytic strabismus: (i) Convergent strabismus: (*a*) accommodative (wholly or in part): orthoptic treatment is valuable in all types, coupled with correction of refractive error and in some cases operation; (*b*) non-accommodative: if of early onset (birth to eighteen months), operation within two or two and a half years of life and no orthoptics; if of later onset (two to three years), operation and then orthoptic treatment may be of great value; if of late onset (three to five years), operation *plus* adequate orthoptic supervision is the treatment of choice; (ii) divergent strabismus: operation is required in most cases; orthoptic treatment alone in a few cases of intermittent divergence will suffice. The treatment of congenital paralytic strabismus is adequate operation at an early age.

OTO-RHINO-LARYNGOLOGY.

Chronic Bacterial Allergy of the Perinasal Sinuses.

J. R. SUTTER (*Arch. Otolaryngol.*, November, 1956) reports on a study of 65 cases. The patients suffered from a wide variety of symptoms, and many conditions such as arthritis, hoarseness, asthma, bronchiectasis, pulmonary tuberculosis, Eustachian catarrh, deafness and vertigo, peptic ulcer, hypertension and cholecystitis were aggravated by bacterial sinusitis. Local symptoms consisted of nasal blockage, sneezing, watery rhinorrhœa, post-nasal discharge and dryness of the throat. Clinical investigation revealed that 75% of sinus infections were caused by *Staphylococcus aureus*. The author states that staphylococcus toxoid may be of great value in controlling allergic and inflammatory symptoms. *Bacillus proteus* and *Pseudomonas pyocyanea* are found, but most important are *Streptococcus viridans* and *S. mitis* (pneumococcus type III). Many strains of these organisms are resistant to antibiotics. The course of the disease may be characterized by a tendency to cyclic reactivation, often precipitated by slight chilling, fatigue or alcoholic indulgence. The patient must always protect himself against such influences. Some help may come from medicinal measures. Dust and pollen extracts, staphylococcus toxoid and autogenous vaccines may help in early cases. Great care must be exercised to keep below the reaction level in giving antigenic material and vaccines. Medical treatment cannot provide drainage of blocked sinuses or remove the hopelessly diseased and thickened mucosa in long-standing cases. For these, surgical measures are necessary. It is possible to operate on the sinuses without destroying functional nasal structures. A Caldwell-Luc operation on the antra, together with transantral ethmoidectomy, is particularly valuable in pansinusitis, yet no functional tissue is lost, as the nasal space itself is not entered. However, septal straightening, infracture of the turbinates, stripping away of polypoid fringes and intranasal ethmoidectomy may reasonably be combined with operation on the antra when necessary.

The Influence of Prednisone on Nasal Polyposis with Anosmia.

W. T. HOTCHKISS (*Arch. Otolaryngol.*, December, 1956) states that there have been reports of favourable effects on nasal allergic states and on the remission of growth or almost complete disappearance of nasal polypi during the course of administration of cortisone, hydrocortisone and corticotropin. However, adverse effects of the drugs have often forced the interruption or discontinuance of treatment. The effect of the newer steroid product prednisone is the subject of the present report, based on a study of 30 patients suffering from nasal obstruction caused by massive nasal polypi. Prednisone was prescribed in the form of one five-milligramme tablet three times a day for three days, then one tablet twice daily for two days, and then one tablet for one day. On the seventh day the patient's nose was reexamined. The shrinkage response was found to be in direct proportion to the fluid content of the polypi. In the case of mucoid polypi the response was dramatic. Almost complete disappearance of the growths had taken place. The sense of smell was restored. The response was less in the fibrous type of polypi. In two patients, mulberry-like posterior tips of the turbinates disappeared. In a few cases the dose was repeated for two or three weeks, but the result at the end of a week or two proved maximal. If, after maximum shrinkage has been attained, the prednisone is discontinued, a reversal

to the original condition is noted in about ten days. A maintenance dose is therefore necessary. The average dose appears to be three milligrammes a day in one-milligramme tablets. If larger maintenance doses are required, the patient must be kept under observation. Prednisone is contraindicated in cases of peptic ulcer, tuberculosis, psychosis and *herpes simplex*. This steroid may produce all the complications of an overdose of cortisone, hydrocortisone or corticotropin, but it does not lead to retention of sodium and water.

The Naso-pharyngeal Fibroma and Its Treatment.

R. T. ACUNA (*Arch. Otolaryngol.*, December, 1956) states that naso-pharyngeal fibromata are prevalent in the Americas, and especially in Mexico. In the general hospital of Mexico City, an average of 12 cases per year has been recorded in the past six years. The pathogenesis of the tumour is not clear. The condition generally develops in males aged between ten and twenty-five years. Although it is a benign tumour, its invasive and destructive tendency is great; it causes serious functional upsets in adjacent structures and exposes the patient to the risk of severe hæmorrhage. The tumour may be located in various sites about the naso-pharynx. As it grows, it descends into the pharynx or invades the nasal pit, obstructing the passages. It has been observed that when the tumour has been caused to rupture, it tends to adhere in the place of rupture to those walls which are nearest to it. Biopsy is a procedure to be used only in cases of doubt, because of the tendency to subsequent hæmorrhage, and because adhesions may follow the interference, making subsequent operation more hazardous. Spontaneous regression at a specific age was observed in only one case; therefore treatment, medical, physical and surgical, was called for. Supernutrition, vitamin administration and the use of male sex hormone were tried without success. Some regression of small tumours was observed to follow irradiation, but there was no appreciable effect when the tumour was large. Surgical treatment is likely to be needed. Intubation of the larynx is essential. Ligature of the external carotids may lessen the hæmorrhage at operation. The patient is placed with the head hanging off the table. Gauze packs of proper size should be ready for use as soon as operation is completed. The approach may be retropalatine, transpalatine, endonasal or transmaxillary, or by lateral rhinotomy, according to the location of the tumour. It was never necessary to resect a portion of the hard palate. Once the tumour has been exposed, it is necessary to isolate it with very gentle movements to avoid rupture and hæmorrhage. Different methods have been tried to remove the tumour. The cold snare gave no good results. The use of good strong forceps has been found to be the most important point. These must not be likely to release their grasp or tear the tumour. Once the tumour is held, moderate and constant traction is exerted, aided by the use of a detacher or long curette, to remove the tumour from points of insertion. The operation must be rapid, as hæmorrhage begins from the first detachment. If any remaining pieces of tumour can be identified, these should be removed immediately. The previously prepared packs should be speedily put in place and will usually stop hæmorrhage with relative ease. These remain in place for twenty-four to forty-eight hours, and may be reinserted if hæmorrhage recurs. Adequate supportive and resuscitative measures should be employed after operation. In the treatment of 60 patients in the past five years, not one death occurred. Occasionally a second operation may be needed to remove fragments of tumour tissue. Small fibromata have been successfully treated by electrocoagulation.

Congenital Bilateral Choanal Atresia.

A. J. CRACOVANER AND M. GOODMAN (*Arch. Otolaryng.*, October, 1956) state that congenital choanal atresia, a rare condition in children, is characterized by closure of the posterior nares by a partition that may be membranous, osseous or membrano-osseous. The condition may be bilateral or unilateral. Many feel that the condition is due to failure of the bucco-nasal membrane to rupture. Others have suggested that atresia is caused by an osseous projection from the horizontal portion of the palate bone. Bilateral choanal atresia in the newborn represents a medical emergency. The salient features are recurrent cyanosis with asphyxia, inability to feed and filling of the nasal cavities with mucus. The child requires constant supervision to keep the mouth open, as this will not be done without aid, the instinctive action being to breathe through the nose. The child must be fed by a dropper until facility is developed to breathe through the mouth, and to eat properly. Diagnosis is confirmed by failure of a probe or catheter to pass into the naso-pharynx. X-ray examinations with radioopaque medium in the nose also reveal obstruction at the back of the nasal cavity. Unilateral or incomplete atresia is usually not diagnosed until later in life, as it does not cause an emergency. In infants the time of surgical intervention is dependent on the degree of respiratory distress. The earliest approach may be by simple trephine, but these soon tend to close. It may be wise to wait for several years before attempting surgery. The transpalatal approach is much favoured, as good visualization is thus obtained of the obstructing tissues and of the posterior end of the septum. A transantral approach also has been described. In cases of intranasal surgery a long post-operative routine of packing, the use of rubber and metal tubes, and frequent dilatations may be needed. In a twenty-two-months-old girl the authors gained access through a "U"-shaped incision towards the periphery of the hard palate. After elevation of the muco-periosteal flap, the muco-periosteum over the posterior aspect of the occlusion was able to be separated. The posterior third of the bony hard palate was next removed and the mucosa then raised from the anterior face of the occluding partition. The posterior third of the septum and the occluding bony plates were then resected, so that the entrance to the naso-pharynx was smooth. The raw, bony surfaces were covered as far as was possible with the elevated mucosal flaps. The incision in the hard palate was sutured. Healing was rapid. The posterior nares remained patent without use of packing or tubing.

Primary Skin Grafting of the Fenestra and Fenestration Cavity.

G. E. SHAMBAUGH, JUNIOR, AND E. R. DERLACKI (*Arch. Otolaryng.*, July, 1956) state that in 88 fenestration operations the usual technique was modified by the use of split-thickness skin grafting of the fenestration cavity with the purpose of hastening epidermization and of distinguishing the frequency and duration of post-operative treatments. Also, in the hope that the possibility of hæmorrhage into the labyrinth and of post-operative labyrinthine reactions might be reduced, the fenestra was covered with a split-thickness skin graft instead of the usual pedicle flap. To this end a wedge was cut in the tympano-meatal flap over the fenestra, the latter being covered with a Thiersch graft. In every case but one the graft over the fenestra survived, and in this case the fenestra ultimately became covered by a thin epithelium without infection or severe damage to the labyrinth. Most of the patients with skin grafting of the fenestra showed less than usual vertigo and nystagmus for the first two or three days, but a number developed some labyrinthine symptoms several days later. There did not appear to be a great difference between the final healing time in the grafted and non-grafted cases. Of the grafted cavities, 26% were still moist after six months, compared with 21% of the non-grafted cavities. The split-thickness skin graft adheres closely to the bone with little subcutaneous tissue. The surface may show a tendency to excessive desquamation. A comparison of the two-year hearing results showed little difference between the two techniques. The method of covering the fenestra with a free Thiersch graft instead of the usual pedicle flap does not decrease the post-operative serous labyrinthitis and should be reserved for cases in which the pedicle flap appears for some reason to be unsuitable.

Objective Audible Clicking in the Ear.

E. M. FREUND (*Arch. Otolaryng.*, August, 1956) describes a type of objective tinnitus in which there is no relationship between the head noise and the pulse beat. There may be no accompanying loss of hearing and no demonstrable ear pathology. The ætiology of this objective tinnitus is not definitely known. It is usually heard as a clicking or ticking noise, and is apparently caused by muscular contractions involving the *levator palati*, the Eustachian muscle fibres, the stapedius or the *tensor tympani* muscle. There may be a history of a facial nerve paralysis at the onset. At times clonic contractions of the soft palate may be evident. The neuro-muscular anatomical basis of these clonic contractions is complex. The motor fibres of the trigeminal, facial, glosso-pharyngeal and vagus nerves may be concerned. The prognosis, so far as it relates to alleviation of the symptom, is rather poor. Nerve section, mastoid surgery, sedatives, antihistamines and amphetamine have been tried.

Clinico-Pathological Conferences.

A CONFERENCE AT SYDNEY HOSPITAL.

A CLINICO-PATHOLOGICAL CONFERENCE was held at Sydney Hospital on January 15, 1957, the medical superintendent, DR. NORMAN ROSE, in the chair. The principal speaker was DR. M. P. SUSMAN.

Clinical History.

The patient was a fifty-seven-year-old housewife, who had lived most of her life in Narrandera, New South Wales. Four uncomplicated pregnancies had produced four healthy children, the youngest being thirty-three years old. At the age of twenty-five years she had an appendicectomy, eighteen months before the present admission to hospital a cholecystectomy, and twelve months before admission a hysterectomy. The present illness commenced at 4 a.m. on the day before her admission to hospital, when she awoke with a severe constant burning pain in the epigastrium. Sometimes severe bouts of pain radiated to the back, and she commenced almost immediately to vomit. She reported to the casualty department, where the pain was relieved by atropine. However, the pain recurred with vomiting and she was admitted next day. At this stage she was vomiting every few minutes, and was in a state of shock with a rapid pulse and low (unrecordable) blood pressure. She had passed no fæces or flatus since the onset of the pain. Somewhat similar attacks of much less severity had occurred occasionally during the preceding few months. These were rarely accompanied by vomiting, occurred mostly at night, and were not related to food intake. Further interrogation revealed occasional bouts of chest pain radiating down both arms and related to effort. She also admitted to breathlessness on exertion and swelling of the feet. She stated that she had had high blood pressure. She had never been jaundiced.

Examination showed that she was an obese woman in obvious distress. The tongue was furred and dry and there was *fœtor oris* (one observer thought the breath smelled like urine). The vomitus was dark, orange-coloured fluid. Generalized abdominal tenderness was present, most pronounced in the epigastrium. No masses were palpable, and there was no rigidity or guarding. The bowel sounds were audible. Digital examination of the rectum revealed no abnormality. The blood pressure taken in the ward was 125 millimetres of mercury, systolic, and 75 millimetres, diastolic, her pulse rate was 132 per minute, and her temperature was 99·4° F. A catheter was passed, but no urine was recovered. No abnormal features were observed in other systems. The hæmoglobin content of the blood was 22 grammes *per centum*, and the serum amylase content was three Wohlegemuth units.

An intravenous infusion of glucose and saline was commenced. A urologist was consulted and recommended the administration of pethidine and morphine as necessary, fluids by the intravenous route, suction drainage of the bowel, and an urgent estimation of the plasma creatinine level. A plain X-ray film of the abdomen showed no fluids, no air under the diaphragm and no calculi. The blood urea nitrogen content was 27 milligrammes per 100 millilitres, the creatinine content 2·0 milligrammes per 100 millilitres, and the carbon dioxide combining power 48 volumes *per centum*. The white cells (11,200 per cubic millimetre) consisted of lymphocytes 38%, monocytes 6% and neutrophile cells 56%, with a "shift to the left" and toxic changes. The outpatient records showed that the patient had achlorhydria and that a recent electrocardiogram was normal. The blood pressure had been 190 millimetres of mercury, systolic, and 100 millimetres, diastolic.

Laparotomy was performed six hours after her admission to hospital, forty-two hours after the onset of her illness. The post-operative course was complicated by acute renal failure, but eventually her recovery was complete.

Clinical Discussion.

DR. M. P. SUSMAN: Dr. Rose, ladies and gentlemen, I shall begin, if you do not mind, back to front, and state the first tentative thoughts that came to me after I had studied the case history. Here, I thought, was a woman with acute stoppage of the bowel, either mechanical or paralytic, with probably some vascular interference with the intestine. The acute lesion we are dealing with I thought was superimposed on something more chronic. She had renal failure on admission which went on to anuria, and this, I thought, had been precipitated by shock, dehydration, infection or a combination of these; and the history shows that she suffered from generalized cardio-vascular disease.

Now, having expressed these preliminary ideas, I would like to discuss what I feel are the significant positive findings. We are dealing with a stout elderly country woman. She has had three abdominal operations, two of them within the last eighteen months. She has had similar attacks to the present one, but less severe, and she was admitted in extreme shock. The vomitus, although not fully described, probably contained some intestinal contents. The pain was epigastric, went to the back and was described as burning. She had epigastric tenderness which later on became generalized. The bowel sounds were present, and the serum amylase index was three units. However, there are many negative signs which are very important and some very serious omissions from the history and the examination. A significant negative finding was that there was no rigidity of the abdomen, and there was no mass palpable, and, in parenthesis, I must remind you that tenderness and obesity can very easily mask a tumour that may be present. But look at all these omissions in the history: no word whatever about the hernial orifices; a rectal examination was made and said to show nothing, but there was no comment on whether or not there was blood or mucus on the examining finger. There is no comment on the urine, and apparently she came to operation completely anuric. There is no indication as to whether or not she had an enema, and if she did have an enema there is no statement as to what was the result of it. The peripheral pulses do not receive a mention. There is no indication as to whether or not she had had any weight loss. Lastly, although she had an intestinal tube passed, there is no comment on what was aspirated and the amount. Now all these negative points seem to me to be almost as important as the positive ones. Having stated my preliminary impressions, and having reviewed what I consider the significant plusses and minuses, I would like to come to my second thoughts.

After reviewing this history several times, I decided that acute hæmorrhagic pancreatic necrosis was the diagnosis that best fitted the clinical picture. The absence of rigidity was noted, and this is often in contrast to the pain and shock in acute pancreatitis. The site of the pain and tenderness would fit in with a pancreatic lesion, and the previous history of gall-bladder trouble is important, as we know that pancreatitis is very commonly associated with diseases of the biliary tract. She was admitted to hospital on her second visit in shock, and shock is common with acute pancreatitis. Against this diagnosis is the fact that the serum amylase was not raised. A rise in serum amylase is an important finding in favour of pancreatitis, but the fact that it is not raised does not exclude it.

The second condition which I would favour is intestinal obstruction associated with some blockage of the blood supply of the gut. I include the element of vascular strangulation, because of the extreme shock which was a prominent finding in this patient. Having thought of intestinal obstruction with strangulation, what conditions does one think of? Well, obviously, a strangulated hernia, first of all, because it is one of the commonest causes of obstruction. But the hernial orifices are not mentioned in the protocol. One must also think of the possibility of an internal strangulated hernia—for example, through the foramen of Winslow or through the diaphragm.

Next I must mention post-operative bands. I do this because of the history of at least three abdominal operations, two of them recently.

Thirdly I will mention mesenteric thrombosis, because it is clear from the history that she had generalized cardio-vascular disease; and because of that I must also mention the possibility of a leaking or ruptured abdominal aneurysm.

I am against that diagnosis, because the woman recovered, although she did not come to operation until forty-two hours after her illness began.

Intestinal obstruction with perforation going on to peritonitis is a possibility; it could account, after forty-two hours, for a clinical picture not dissimilar to that described. In a woman of fifty-seven, common lesions are carcinoma of the colon and diverticulitis of the colon. These as well as most of the other conditions I have mentioned are compatible with some previous abdominal discomfort. I exclude volvulus of the gut, since it is generally associated with extreme abdominal distension and vomiting is apt to be late. Other possibilities are intussusception and obstruction from a foreign body—for example, a gall-stone or undigested food; at the end of forty-two hours such an intraluminal obstruction could produce the clinical picture described.

Perforation of a peptic ulcer is a possibility; I entertain this diagnosis only because of the forty-two hours' history.

Now in Australia, especially in a person from country districts, one must always think of the possibility of a hydatid cyst. I do so here only because it is frequently overlooked as the cause of a patient's illness. A hydatid cyst, when it ruptures, may cause profound shock and death. A hydatid cyst, according to its site, can rupture into any tissue or into a viscus, into a serous cavity or into a blood vessel. So rupture of a hydatid cyst could produce a picture similar to that described here. Important points against it, but not excluding it, are the absence of eosinophile cells in the blood and the absence of skin rash.

To conclude, I think that this patient was suffering either from acute pancreatic necrosis or from intestinal obstruction, possibly with interruption of the blood supply of the bowel. I agree that operation was advisable; but I should have waited for some resuscitation.

For such exploratory operations I like a transvere incision below the umbilicus across both recti, and if necessary into both flanks. This gives a very good exposure to all parts of the abdominal cavity, and allows the surgeon to deal with almost any condition that may be found. It is especially valuable for emergency procedures when adequate assistance is unavailable, as it gives good exposure with a simple self-retaining retractor. If the diagnosis of pancreatitis was correct, I would probably have regretted operating; I do not think that any patient has recovered from acute pancreatitis because of the operation, but some may have died because of it.

However, in this case the possibility of intestinal obstruction is so likely that operation is indicated.

DR. N. ROSE: Thank you. Before admissing discussion of this case I feel that Dr. Susman should have the benefit of any further information that may be available. Dr. Hirst, have you any further details that may be of help?

DR. E. HIRST: I will endeavour to answer any questions. Meanwhile, in reply to the points made by Dr. Susman I have to state the following: Mention of the hernial orifices was not made in the history. No information can be found regarding the further findings on rectal examination. Whether or not an enema was given was not stated, and similar remarks apply to weight loss and to the type of fluid withdrawn in the aspirate.

DR. ROSE: I will call for any comments from the audience.

DR. W. L. CALOV: This is a patient with vomiting, shock and abdominal pain. There are many diseases that can cause these symptoms. In my opinion the diagnosis was between acute hæmorrhagic pancreatitis and a ruptured viscus. I favoured pancreatitis because the vomiting continued. I may be in error, but my feeling is that when a viscus ruptures the patient vomits promptly and copiously, but after that the vomiting ceases. I have used this fact as an aid to the differentiation of ruptured viscus and hæmorrhagic pancreatitis, and in view of this I think that of those two the probability is that of pancreatitis, but I would prefer to hear other opinions. There is, however, one other possibility, and one that physicians are not infrequently asked to determine. That is acute myocardial infarction. I think that this was not a case of myocardial infarction, and probably it is far more complicated, and I fear that there may be a catch somewhere. It is obvious that it was a difficult case, in which the surgeon concerned was in doubt and thought he would look and find out; I hope he did find out, or we shall never know.

DR. W. EVANS: It seems to me that the diagnosis should be approached as Dr. Susman has done, from the point of view of whether there is a general cause or a local one. The first condition that crossed my mind was the possibility of lower nephron nephrosis due to ureteral calculi. But when one sees the results of the investigations, especially the blood urea, and that they are normal, I feel that this can be excluded. There is no other likely general cause. One considers then the local causes—conditions such as Dr. Susman has suggested—for example, acute pancreatitis, an obstruction in the bowel itself or an embolus. In dealing with the last one first, I think it is unlikely, because the patient had had several attacks previously, and it is unlikely that she had several attacks of mesenteric vascular occlusion. In regard to acute pancreatitis, I must admit I am not in agreement with the two previous speakers. I think that if she had acute pancreatitis the serum amylase would have been raised, and also that, although there was generalized abdominal tenderness, there also would have been some mention of rigidity. Although acute pancreatitis is not generally associated with board-like rigidity, in my experience here I have found that it is confused with intestinal obstruction or a ruptured ulcer, and there is some degree of rigidity. The three or four previous attacks also are somewhat against this diagnosis of acute pancreatitis. So I consider the most likely possibility is that of some kind of intestinal obstruction, either with the bowel being obstructed by an adhesion or by blockage due to carcinoma or volvulus. Volvulus is unlikely because of the absence of distension or a palpable mass, and in addition to that, the condition appears to be small rather than large bowel obstruction, since there is no great intestinal distension. However, there is acute vomiting, which favours an obstruction of the small bowel. So in my opinion the probability is either carcinoma or small bowel obstruction by herniation beneath an adhesion. The last possibility is a dissecting aneurysm, since this may by dissection obstruct renal vessels causing anuria. This is easily excluded by noting that the patient recovered.

DR. H. S. H. WARDLAW: With reference to the figure for serum amylase, the fact that this figure is within normal limits is not necessarily evidence against a diagnosis of acute pancreatitis. The raised level of serum amylase in this condition may be of brief duration and could easily be missed.

DR. R. M. RAWLE: I find this case extremely complex. Acute pancreatitis is, I agree, the most obvious diagnosis. The patient had some previous attacks, which could be interpreted as mild attacks of pancreatitis. But they had never been related to food, and there is further an absence of a history of indigestion since her cholecystectomy. Another point is that if this were acute fulminating pancreatitis, I would have thought, in view of the activity of the disease at this stage, that the amylase index would have been raised. While agreeing that a rise in the index may be transient, the story gives the impression that the disease was still in the active stage, and the finding of the normal serum amylase to me weighs against that diagnosis. Another point of importance to me is that the story, although at least thirty-six hours old, contains little evidence of abdominal distension. In acute pancreatitis the colon becomes very grossly distended, and one would expect to find absent bowel sounds, whereas in this case they were present. In view of these features I would look for other likely causes, and I would entertain, as mentioned before, a high intestinal obstruction. This could give rise to the symptoms of dehydration, fall in blood pressure, anuria *et cetera*, and in that connexion one notices that she commenced to vomit almost immediately, which is again in favour of a very high intestinal obstruction. So that one wonders whether the obstruction is very high, and this brings to mind the possibility of an obstruction in an hiatus hernia. As mentioned by Dr. Susman, one must seriously consider the diagnosis of obstruction in an hiatus hernia.

DR. K. B. NOAD: I think that this patient had a high intestinal obstruction, and I think that the cause could be a neoplasm. Because she had a history of attacks over the preceding months, it appears to be a story of something progressive—a process culminating in this extremely severe attack which (and I draw attention to this fact) was relieved by atropine. Now I cannot see how, if she had pancreatitis, it could be relieved by atropine. The casualty officers were satisfied that the attack had been relieved, and this suggests, since she had been allowed to go, that the attack was one of spasm of a hollow viscus—a muscular tube. I would think that the rest of the story indicates that the bowel was the most likely structure to be affected. As had been pointed out, she felt the pain and commenced to vomit. This suggests a high intestinal obstruction. Although neoplasm in the small bowel is rare, the nature of the story suggests that she had a high intestinal obstruction associated with a new growth.

DR. ROSE: Assuming that this patient had been in your care, Dr. Billington, what measures, in your opinion, should have been taken?

DR. B. P. BILLINTON: If I had charge of this patient, I would call a surgeon to operate on this patient and elucidate the diagnosis. In my opinion the diagnosis is not obvious from the history on the protocol. Each of the possibilities mentioned has occurred to me, and I have no firm opinion as to what the diagnosis may be in this case. Furthermore, it seems that the surgeon, too, at the time, did not know the precise diagnosis, and that is probably the reason why the operation was performed.

DR. ROSE: Could you mention any investigation which may have been of help in indicating the diagnosis?

DR. BILLINGTON: I think that they would only have amounted to undesirable delay.

DR. ROSS: Thank you for the discussion. It is noticeable that the problem of the pre-operative and post-operative anuria has not been discussed in detail. This may be better discussed after disclosure of the operation findings.

DR. E. HIRST: The pre-operative diagnosis was high intestinal obstruction. The abdomen was opened by a four inch upper mid-line abdominal incision. The jejunum and ileum were found to be dilated. Situated approximately 18 inches from the ileo-caecal junction, a firm mass was palpable in the lumen of the ileum. Below this point the remaining ileum and large bowel were of normal calibre. By manipulation the mass was pushed proximally for a few inches and a longitudinal incision was made over it. The obstructing material was thought to be a mass of orange pulp. The bowel was closed in two layers, the inner with continuous chromic gut and the outer by interrupted silk sutures.

The pathologist received a mass of orange-coloured pulp about 5·0 by 2·5 by 1·5 centimetres and weighing eight grammes. Microscopic examination showed this to be composed of plant fibres. The diagnosis is therefore intestinal obstruction proximal to the ileo-caecal valve by a mass of orange pulp.

Discussion.

DR. H. M. WHYTE: On the day of her operation this patient passed no urine, her hæmoglobin value was 22 grammes, the blood pressure 110-125 systolic and about 70 diastolic (which is considerably lower than before the present episode), and she was given intravenously about three litres of fluid made up of glucose-saline, Darrow's solution and Ringer's solution. The blood urea nitrogen was 27 milligrammes per 100 cubic centimetres, the creatinine 2·0 and the carbon dioxide 47 volumes. On the second day she passed 150 cubic centimetres of urine, the hæmoglobin was 14 grammes and she was given blood and Ringer's solution. On the third day she passed 590 cubic centimetres, on the fourth, 470 cubic centimetres, and thereafter, 1050 cubic centimetres, *plus* more into the bed, 1200, 1080, 2250 and 2490 cubic centimetres on the ninth day.

It is quite clear that this patient did suffer post-operatively for two days from acute renal failure—that is, the kidneys failed to excrete more than 400 cubic centimetres of urine daily, which is considered to be the minimum volume into which the daily waste substances can be concentrated. It was not till the fifth day that the urinary output exceeded one litre. Renal function depends on a proper blood supply, glomerular filtration, tubular reabsorption and free passage for urine, so that if the blood supply is inadequate, glomerular filtration deficient, tubular reabsorption excessive or the urinary tracts blocked, one might expect the kidneys to fail in their task of passing at least 400 cubic centimetres of urine per day. The commonest cause among these is excessive tubular reabsorption, which occurs when the tubules have been damaged, as during a period of anoxia which leads to acute tubular necrosis, the condition originally called lower nephron nephrosis. Circulatory insufficiency is one of the conditions which can cause this condition, and probably did so in the case under discussion today. It is obvious that she was dehydrated.

The kidney normally plays a part in fluid balance, acid-base regulation, the excretion of wastes and the adjustment of the bodily contents of salts. There is a danger in anuria, therefore, of over-hydration, acidosis, uræmia and various electrolyte disturbances, particularly hyperpotassæmia. Luckily, in this case the period of anuria was short, and these complications were not marked. But when anuria or oliguria is first detected, it is not possible to guess how long the trouble will continue, so that it is important that proper treatment should be commenced immediately. In fact, treatment should begin before renal failure occurs, with prophylaxis, attempting to prevent shock and dehydration in a case such as this. Once the kidneys have failed, it becomes a matter of sustenance, to provide sufficient water but not too much, and sufficient food. The daily requirement of water is 400 millilitres *plus* any overt losses. The food should contain no protein, no potassium, no sodium, and it should provide up to 1000 Calories per day as carbohydrate and fat together with vitamins. If any of the dangers of renal failure become real, then corrective treatment has to be given—for example, fluid restriction for over-hydration or by using an artificial kidney for removing excess acids, urea *et cetera*. Emergency treatment for hyperkalæmia might include the giving of glucose and insulin, ion exchange resins, digitalis, calcium or, again, the use of an artificial kidney. Otherwise symptomatic treatment is called for headaches, fits and other complaints. None of these had to be considered in the present case, because of the short duration of renal failure.

Nor did the diuretic phase assume the proportions it sometimes does following oliguria, when it can become very dangerous, bringing various complications with it, and calls for careful treatment in regard to water, potassium and sodium balance.

In retrospect, then, this patient suffered a brief period of renal failure, probably due to acute tubular necrosis induced by circulatory insufficiency associated with dehydration and shock. Being brief, no special treatment was indicated and recovery was uneventful. But in all such situations the possibility of a prolonged period of oliguria should be considered and appropriate treatment commenced early, rather than leaving it till later when corrective treatment becomes so much more difficult.

Diagnosis.

Intestinal obstruction proximal to the ileo-caecal valve by a mass of orange pulp.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

TOUTING BY QUALIFIED MEN.[1]

[From *The Australasian Medical Gazette*, February, 1885.]

OUR attention has been called to the fact that more than one member of the profession in these Colonies is in the habit of distributing printed circulars containing complimentary testimonials as to his professional abilities: in some instances this has been done personally by the practitioner himself. These men who have so little sense of the dignity of the profession to which they belong and whose advertising and commercial instincts are so strongly developed as to necessitate their touting for employment, have good grounds of complaint against their guardians in forcing them unnaturally into a learned profession when they are so much better fitted for the calling of a cheap grocer or draper in which their advertising talent could be so legitimately and advantageously employed. Amongst the sinners is one who fills an honorary appointment in one of the leading hospitals in Australia. It is to be regretted that the public do not sufficiently realize the fact that the higher the professional attainments of the practitioner and the greater the mental capacity and sense of honour which he possesses, the less likely is he to resort to such derogatory means of letting his attainments be known, and that nothing really is a greater proof of the inferiority of the man than that he finds it advisable to publish what other more refined men probably possess but do not find it necessary to trumpet forth.

Correspondence.

BOLUS OBSTRUCTION AFTER PARTIAL GASTRECTOMY.

SIR: After reading reports on the subject of intestinal obstruction following partial gastrectomy, I have noted that little or no comment is made on a cause which deserves more attention.

After partial gastrectomy there are many ways in which intestinal obstruction may develop, especially in the gaps around the anastomosis. F. A. Stammers[2] has adequately described this problem in a large series. It would be interesting to know the real incidence of bolus obstruction after partial gastrectomy.

[1] From the original in the Mitchell Library, Sydney.

[2] *Ann. Roy. Coll. Surgeons England*, 1955, 17: 373.

In the subject who fails to gain weight after partial gastrectomy, presumably due to intestinal hurry and poor fat absorption, it would seem reasonable that the "hurry factors" would encourage bolus formation. Also, in those cases where a large stoma was present, such as in the Pólya procedure, a food bolus would more readily develop and threaten obstruction of the small gut. We usually advise our patients after partial gastrectomy to "eat little and often", but perhaps we should also add "chew well and don't gulp".

The following account of a case illustrates the problem. A painter, aged fifty-two, was admitted to the Mater Public Hospital on July 13, 1956, with the classical picture of small gut obstruction. The patient gave a history of partial gastrectomy for chronic duodenal ulcer five years previously. Laparotomy revealed a large bolus firmly impacted in the lower ileum; this was easily removed by enterotomy. On close examination, the bolus, about three inches by two inches, was found to consist of the undigested pieces of a chicken and ham roll. When confronted with the news of the nature of his bowel obstruction, the patient recalled eating such rolls a few days previously whilst enjoying his grandson's christening party.

The patient was very thin and had suffered considerable loss of weight following partial gastrectomy, which suggested the possibility that he was the subject of "intestinal hurry". It is difficult to understand why such incidents are not more common, but perhaps many cases who, following their gastrectomy, complain of occasional attacks of abdominal pain and nausea, may be the victims of bolus subacute obstruction.

This subject deserves closer study.

Yours, etc.,

Wickham Terrace, Brisbane, Undated.

DANIEL LANE.

GUAIACOL-GLYCERYL-ETHER: A TRANQUILLIZING DRUG.

SIR: I was very interested to read Dr. D. Vann's letter on the use of guaiacol-glyceryl-ether in psychoneurotic and psychosomatic cases, mainly as a physical aid to psychotherapy. In large doses, guaiacol-glyceryl-ether has an effect very similar to mephenesin, and indeed, closely resembles mephenesin in structure. Though in the past it has been used for treating spastic conditions affecting skeletal muscle, it was found that large doses are required to produce the necessary relaxant effect. To date, investigations have revealed that the main therapeutic value of guaiacol-glyceryl-ether lies in its potent expectorant effect, together with its valuable antiseptic and mucus-liquefying properties. Consequently, it was for this purpose that the preparation was introduced for use in Australia.

Yours, etc.,

H. QUINN,
Acting Manager, The Crookes Laboratories Limited.

458-468 Wattle Street, Ultimo, New South Wales.
June 14, 1957.

AGING AND OSTEOARTHRITIS.

SIR: Under the heading "Aging and Osteoarthritis" in the "Current Comment" section of THE MEDICAL JOURNAL OF AUSTRALIA, May 25, 1957, F. Bohatirchuk apparently postulates that the weight of the skelton in humans is not entirely responsible for the appearance of osteoarthritic changes in old age. I quite agree, and have maintained for many years that osteoarthritis, especially in the spine, is conditioned originally by physical and emotional stress and strain.

In the routine procedure during the past thirty years of having every case X-rayed, again, principally those showing predominantly spinal symptoms, I have come to the conclusion that the trouble most frequently begins in the cervical spine, which is liable to a great deal of movement, and often strain, but which carries only the weight of the head.

As far as the weight of the spine is concerned, animals have to carry the longitudinal burden of weight of a fairly long spine. Animals—*e.g.*, dogs and horses—are also very subject to anxiety states and nervous tension, and occasionally physical stress.

As for normal versus morbid changes in old age, many people show osteoarthritic changes, such as osteophytes, without any painful symptoms, and a great many patients, young and old, suffer considerable pain and disability without any pronounced radiological pathology. These are the cases in which ligamentous and muscular tension plays such a large part, and which so often is the forerunner of bony changes, and which are principally psychosomatic. In these instances one frequently sees a belt or a brace prescribed, a type of appliance which mostly should be relegated to the scrapheap, being at worst a psychological crutch and a placebo, or at best an inefficient and uncomfortable form of splint.

In pathological descriptions of osteoarthritis, it is still hard to better Lawford Knaggs, "Inflammatory and Toxic Diseases of Bone" (published by Wright, Bristol, 1926). Anyone who attempts to treat these cases—and there are many who aspire, but few who succeed—must incorporate in their therapy not alone the physical aspect, but most essentially, the psychosomatic.

Yours, etc.,

231 Macquarie Street, Sydney,

E. HASLETT FRAZER.
June 11, 1957.

TRAINING IN SURGERY.

SIR: The late E. S. Meyers[1] discussed the above subject on occasions in the past. Time did not permit all of his ideas to reach print. It was his wish that these be made known when and where it appeared appropriate. Your editorial,[2] "Surgery at the Periphery", reopens this subject.

To place his opinions in proper perspective will require brief reference to some of his earlier comments. He considered[3] that: (*a*) Planning was necessary. (*b*) "Post-graduate surgical education is a matter that affects Australia as a whole, and there should be set up, preferably by the Federal Government, hospitals for post-graduate teaching in each State . . . with a permanent teaching staff . . . not engaged in . . . extensive undergraduate . . . teaching."

Of today's undergraduate training for surgery in general practice he wrote:[4] "The bachelor of surgery degree should not be awarded on graduation but only the degree of bachelor of medicine. The general practitioner-surgeon should be required to take a bachelor of surgery degree, and should be trained as a graduate in those procedures which are part of everyday surgery by gaining the necessary experience in a hospital working under the guidance of a qualified surgeon."

To the subject of the training of the specialist surgeon his remarks concerning post-graduate hospitals apply. Of the three-year surgical fellowships available in certain medical centres in the United States of America, he considered that although their systems should not be followed slavishly here, there was much that could be learnt from them.

It was to the question of establishment of conditions wherein the practising doctor might acquire necessary additional knowledge and skills, diagnostic and technical, that the late E. S. Meyers latterly had turned his attention. He awaited the opportunity to develop ideas which may be expressed along the following lines: (i) A plan must be found to make it possible for country and suburban practitioners to undertake special "fellowships" for varying periods of three to six months. In such a period the practitioner would follow a planned course of study, seminars *et cetera*, and would be attached to a particular teaching specialist to pursue the academic and technical aspects of his chosen work. (ii) Practical methods must be found whereby the practitioner (especially the solo practitioner) would be able to maintain his family and provide a *locum tenens* for his practice for the period concerned.

For the latter purpose he believed that the following ideas should be investigated by competent advisers: (*a*) That a contributory fund (perhaps subsidized), suitably invested, be established from which the payment of locums might be possible. (*b*) That alternatively, or complementarily, the

[1] M. J. AUSTRALIA, 1956, 1: 944.
[2] *Ibidem*, 1957, 1: 515.
[3] *Ibidem*, 1948, 1: 193.
[4] *Ibidem*, 1953, 2: 913.

locum be provided by exchange with a hospital registrar, such extra complement of registrars necessary to be an integral feature of the post-graduate or major hospital concerned. (c) That the practitioner receive a stipend from a fund subsidized by Federal grants, State allocations *et cetera*.

He envisaged that in some States new legislation would be required to enable the university concerned to undertake the graduate teaching envisaged for the bachelor of surgery degree; and that such legislation should be well considered and well timed. To this end he believed that the Commonwealth Government, expertly advised, could play a steadying and supportive role in the action to be taken by the several States.

He was convinced of the need for and desirability of Federal financial endowment for post-graduate medical training in general—in the manner exemplified by the British Universities' Grants Committee.

In agreement with the writer of your editorial, the late E. S. Meyers also believed that the professional bodies in each State should send to a specially convened meeting representatives who, having studied in detail the local differing problems of the several States and comparable matters in Canada and in the United States of America, should determine the fundamental principles on which the various relevant aspects of surgical training should be based, and that, when these principles were approved by the bodies concerned, the governments should be advised accordingly and their active and coordinated assistance, in the interests of patients in particular and the community in general, be enlisted.

I would point out that this letter is written in a private capacity and in no way represents the views of any official or section of any university, hospital or governmental department.

Yours, etc.,

June 14, 1957. "R.M.".

WILLIAM HARVEY, 1578-1657.

SIR: When the tercentenary of William Harvey (June 3, 1657) ended over three hundred years of exact knowledge of the heart and thirty years of "cardiology", perhaps too little emphasis was placed on the fact that William Harvey achieved the transformation of our outlook on the material nature of human life, by putting an end to Aristotelian and Galenic physiology.

We now know that the best of hearts can do no more than pump out through the arteries and receive back from the veins ten gallons of blood each minute to keep the body working. The heart does not "know its own bitterness", nor does it "leap for joy"; it simply pumps blood, and Harvey's miserably printed Latin booklet *"De Motu Cordis"* convinced us, although the loom of language had woven into the fabric of our speech the idea that the heart is the reservoir of our emotions, and there in our everyday speech the idea remains. Our very character was thought to depend on our heart. People who are generous and kindly "have their heart in the right place". We are "soft hearted", "hard hearted", "broken hearted", "kind hearted", "stony hearted", "heartless" or "have a change of heart". Examples are too numerous to list. It seemed outrageous for William Harvey to prove to his academic contemporaries that the heart is a mere pump when everyone "knew" that the heart was there to distil emotion of our "vital spirit" in the arteries. So he wrote in Latin and published his book in Germany to avoid offending the followers of Aristotle and Galen. In this he opposed the universities of his day and the whole authority of the ancient world.

Of other points unemphasized by his learned biographers in your columns, he settled in London after his marriage to the daughter of a physician to Queen Elizabeth I (she had many, but like Billy Hughes's secretaries, none lasted long), and he became Censor of the Royal College of Physicians, but he declined the Presidency at the age of seventy-six. With the characteristic humility of the great he said he was too old. He and Vesalius are the two practising doctors who have made really immense additions to medical knowledge, but their contributions are so overwhelming that they atone for all of us. He gave part of his estate for medical education and part to provide a librarian to the Royal College of Physicians. In short, he was a typical example of that combination of supreme creative intelligence and philanthropy that England, possibly more often than any other country, has occasionally produced to determine the future of mankind. "Every little breeze seemed to whisper Louise" to the older physician, but antibiotics have altered all that, so, to avoid heart failure, any cardiologist may now advise a life spent completely under the influence of alcohol. ("Heavy indulgence in alcohol over many years has seemed to afford this protection"—Cecil and Loeb, the classical American "Text Book of Medicine", 1935.) However, a diet of lettuce, nuts and hominy, to reduce the blood fat level, and a regular injection of an anti-clotting drug (suitably checked), as well as a life devoid of emotional stress and excitement, may be equally useful. After a month of that regime and who wouldn't agree with the apocryphal *Ecclesiasticus*?

He that sinneth before his maker,
Let him fall into the hand of a physician.

Yours, etc.,

607 New South Head Road, Rose Bay, New South Wales. GODFREY HARRIS.

June 15, 1957.

Naval, Military and Air Force.

APPOINTMENTS.

THE following appointments, changes *et cetera* are promulgated in the *Commonwealth of Australia Gazette*, No. 29, of May 23, 1957.

NAVAL FORCES OF THE COMMONWEALTH.

Permanent Naval Forces of the Commonwealth (Sea-Going Forces).

Resignation.—The resignation of James Patrick Turner of his appointment as Surgeon Lieutenant (for Short Service) is accepted, dated 21st March, 1957.

Confirmation in Rank.—Surgeon Lieutenant (for Short Service) (on probation) Harold Lindsay Thompson is confirmed in the rank of Surgeon Lieutenant (for Short Service), with seniority in rank of 20th February, 1956.

Citizen Naval Forces of the Commonwealth.

Royal Australian Naval Reserve.

Promotions.—Surgeon Lieutenant Lindsay Henry Jones is promoted to the rank of Surgeon Lieutenant-Commander, dated 27th April, 1957.

Honorary Rank.

Promotion.—Honorary Surgeon Commander James Aloysius Foedus Flynn is promoted to the honorary rank of Surgeon Captain, dated 20th March, 1957.

AUSTRALIAN MILITARY FORCES.

Citizen Military Forces.

Northern Command.

Royal Australian Army Medical Corps (Medical).—1/39164 Captain (provisionally) I. R. Ferguson ceases to be seconded whilst in the United Kingdom, 18th March, 1957. The provisional rank of 1/46764 Captain A. J. Kerr is confirmed. 1/46983 Captain (provisionally) A. J. J. Emmett relinquishes the provisional rank of Captain, 19th March, 1957, and is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Northern Command) in the honorary rank of Captain, 20th March, 1957.

Royal Australian Army Medical Corps (Medical).—1/28390 Major I. H. Chenoweth is appointed to command 9th Field Ambulance, and to be Temporary Lieutenant-Colonel, 20th May, 1957. F1/1017 Captain M. R. Edye is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Northern Command), 27th March, 1957.

Eastern Command.

Royal Australian Army Medical Corps (Medical).—To be Major, 27th March, 1957: 2/165473 Captain J. E. D. Goldie.

Royal Australian Army Medical Corps (Medical).—2/206952 Lieutenant-Colonel J. Loewenthal is appointed Consultant Surgeon, Army Headquarters, and to be Colonel, 12th April, 1957.

Royal Australian Army Medical Corps (Medical).—2/130118 Honorary Captain D. J. Roebuck is appointed from the Reserve of Officers, and to be Captain (provisionally), 14th March, 1957. 2/101562 Major J. V. Roche is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Eastern Command), 22nd November, 1956. To be Lieutenant-Colonel, 15th June, 1954: 2/206952 Major (Temporary Lieutenant-Colonel) J. Loewenthal. To be Temporary Major, 18th April, 1957: 2/127046 Captain R. K. Reid.

Southern Command.

Royal Australian Army Medical Corps (Medical).—3/52326 Lieutenant-Colonel J. N. Freedman, E.D., is placed upon the Retired List (Southern Command), with permission to retain his rank and wear the prescribed uniform, 4th April, 1957.

Western Command.

Royal Australian Army Medical Corps (Medical).—To be Captain (provisionally), 5th April, 1957: 5/45851 Geoffrey Harold Hingston.

Royal Australian Army Medical Corps (Medical).—5/32269 Captain (provisionally J. B. O'Brien relinquishes the provisional rank of Captain, 21st March, 1957, is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Western Command), and is granted the honorary rank of Captain, 22nd March, 1957.

Reserve Citizen Military Forces.

Royal Australian Army Medical Corps (Medical).

Northern Command.—To be Honorary Captain, 1st January, 1957: John Francis Scanlan, M.C.

Central Command.—To be Honorary Captain, 5th April, 1957: Evan Charles Hallett.

The following officers are placed upon the Retired List (Western Command) with permission to retain their rank and wear the prescribed uniform, 20th March, 1957:

Western Command.—Lieutenant-Colonel R. W. Johnson, Majors S. L. Mainland, O.B.E., and K. H. Tepper, and Captain R. H. F. Rockett.

The following officers are retired:

Western Command.—Honorary Lieutenant-Colonel D. A. Quinlan, and Honorary Captains H. E. H. Ferguson and Sir T. W. Meagher, 20th March, 1957.

Honours and Awards.

The following Honours and Awards are made in connexion with the Australian Military Forces:

The Australian Efficiency Decoration.

3/157151 Lieutenant-Colonel (Temporary Colonel) Henry Anthony Phillips, Royal Australian Army Medical Corps (Medical).

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

REFRESHER COURSES, AUGUST AND SEPTEMBER, 1957.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that a limited number of vacancies have been reserved for non-members to attend the following refresher courses on enrolment through the Post-Graduate Committee:

Royal North Shore Hospital, August 12 to 16.

The Royal North Shore Hospital "Reunion Week" will be held from Monday to Friday, August 12 to 16, 1957, full time. The guest speaker will be Mr. A. Dickson Wright, Surgeon to St. Mary's Hospital and Prince of Wales Hospital, London. The fee for attendance is £5 5s., and programmes are now available.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JUNE 15, 1957.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	..	3(1)	..	1(1)	..	..	..	4
Amœbiasis	..	..	..	..	1	..	..	..	1
Ancylostomiasis	..	..	..	..	..	..	..	..	..
Anthrax	..	..	..	..	..	..	..	..	..
Bilharzias	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	11(5)	13(13)	2	..	..	3	2	31	
Diphtheria	2(2)	1(1)	1	..	..	..	..	..	4
Dysentery (Bacillary)	..	..	..	..	..	..	..	..	..
Encephalitis	..	1(1)	..	..	..	..	..	..	1
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	49(18)	25(7)	..	2(2)	0(2)	15(1)	..	2	102
Lead Poisoning	..	..	1	..	..	..	..	..	1
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	2(1)	..	..	..	..	..	2
Malaria	..	1(1)	1	..	..	..	1	..	3
Meningococcal Infection	4(2)	1(1)	1	..	..	..	..	1	7
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	4(3)	..	..	..	1	..	..	..	5
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	29(14)	..	13(4)	2(2)	..	..	4	48
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	14(8)	19(14)	5(4)	15(12)	5(4)	2	..	..	60
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	2	..	..	..	2
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	21(13)	14(9)	13(10)	13(11)	5(2)	6(1)	5	..	77
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

Sydney Hospital, September 9 to 13.

The Refresher Week conducted by the Old Sydney Hospitallers' Club will be held from Monday to Friday, September 9 to 13, 1957, full time. The guest speaker will be Professor John Hayden, of Melbourne. The fee for attendance is £5 5s., and programmes are now available.

Royal Prince Alfred Hospital, September 13 to 20.

The Royal Prince Alfred Hospital Medical Officers' Association will be holding its "Reunion Week" from Friday to Friday, September 13 to 20, 1957, full time. The McIlrath Guest Professor for 1957 will be Professor C. A. Wells, Professor of Surgery in the University of Liverpool. The fee for attendance will be announced later.

Method of Enrolment.

Non-members wishing to attend these courses are requested to make direct application to the Course Secretary, The Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney, from whom further details may be obtained. Telephones: BU 4497-8. Telegraphic address: "Postgrad Sydney."

Courses for Part I of the D.A., D.G.O., D.L.O. and D.O.

Courses for Part I of the D.A., D.G.O., D.L.O. and D.O. diploma examinations of the University of Sydney will be held from September 2 to November 15, 1957. Lectures and demonstrations will be held in the afternoons only, the fee for attendance at each course being £36 15s. Further particulars and copies of the by-laws and regulations governing these medical diplomas may be obtained on application to the Course Secretary, The Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney.

Notice.

RADIATION SOCIETY.

A RADIATION SOCIETY has been formed in Melbourne with the object of encouraging and coordinating work with radiation. Membership, the fee for which is 5s., is open to all interested.

The following meetings have been arranged: Tuesday, July 23, 1957: "Units for Measurement of Radiation", K. H. Clarke, M.Sc., A.R.C.S., A.Inst.P., Physics Department, Cancer Institute Board. Tuesday, September 10, 1957: "Dose Effect Relationship: I, Simple Organisms", A. M. Clarke, Ph.D., M.Sc., Zoology Department, University of Melbourne; 'II, Complex Organisms", H. A. S. van den Brenk, M.B., B.S., D.T.R., M.C.R.A., Cancer Institute Board. Tuesday, December 10, 1957: "Relative Biological Efficiency", a symposium. Tuesday, March 11, 1958: To be arranged.

The convener of the Society is J. H. Martin, Cancer Institute Board, 488 Little Lonsdale Street, Melbourne, C.1, Victoria.

Australian Medical Board Proceedings.

NEW SOUTH WALES.

THE following additions and amendments have been made to the Register of Medical Practitioners for New South Wales in accordance with the *Medical Practitioners Act*, 1938-1957:

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (1) (a) of the Act: Dyer, Henry Paul, M.B., B.S., 1949 (Univ. Queensland); Gudkovs, Ariss, M.B., B.S., 1955 (Univ. Adelaide).

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (1) (b) of the Act: Kirkwood, Eric David Glover, M.B., Ch.B., 1942 (Univ. Liverpool); Manners, John Michael, M.B., Ch.B., 1953 (Univ. Leeds).

Nominations and Elections.

THE undermentioned have applied for election as members of the Victorian Branch of the British Medical Association:

Dennehy, Constance Marguerita, M.B., Ch.B., 1955 (New Zealand), Royal Children's Hospital, Carlton, Victoria.

Koehne, Ivan Harold, M.B., B.S., 1956 (Univ. Adelaide), 214, 12th Street, Mildura, Victoria.

Medical Appointments.

Dr. P. T. J. C. P. Warner has been appointed Medical Research Fellow in the Institute of Medical and Veterinary Science, Adelaide.

Dr. C. P. V. Evans has been appointed Assistant Director of Tuberculosis, Chest Clinic, Department of Health and Home Affairs, Brisbane.

Diary for the Month.

JULY 9.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
JULY 9.—New South Wales Branch, B.M.A.: Organization and Science Committee.
JULY 12.—Tasmanian Branch, B.M.A.: Branch Council.
JULY 12.—Queensland Branch, B.M.A.: Council Meeting.
JULY 15.—Victorian Branch, B.M.A.: Finance Subcommittee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, B.M.A. House, 88 L'Estrange Terrace, Kelvin Grove, Brisbane): Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

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